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ANESTHESIA BY COMBINED INTRAVENOUS PENTOTHAL SODIUM AND LOCAL NERVE BLOCK*

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ANESTHESIA and anesthetic methods have properly concerned the surgical profession as its technical procedures have been perfected. Without adequate anesthesia, an otherwise ideal technical procedure is a matter of trial to the surgeon and a physiologic burden to the patient. Yet the acceptance of anesthetic methods by the surgeon for application to his patients reveals a curious picture of diversity and sectionalism. As far back as 1922 an editorial in the *Lancet*[1] posed this unanswered query: "It would be interesting to ascertain why it is that in England and America general anesthesia has been developed at the expense of local, while on the Continent the reverse process has taken place." Gorth,[2] in reporting a clinical trip abroad for the study of anesthetic methods, as late as 1938 made the following interesting observations:

> Anesthesia on the Continent has lagged behind anesthesia in the United States. . . . Recently, however, a large number of Continental clinics are using intravenous anesthesia extensively not only for minor and short operations, but for all kinds of surgery. . . . However, it may be that they are really setting the pace for us rather than going off at a tangent as it now appears. . . . With modifications, then, such as the use of Pentothal during the induction of the splanchnic block, it seems we might perhaps do well to follow Finsterer in our handling of upper-abdominal surgery.

In America there is now a distinct sectionalism in the use of intravenous Pentothal Sodium for major surgical procedures. Reports from some sections indicate marked enthusiasm for its employment for all types of surgical cases, of whatever magnitude. These reports seem at times to lack careful and forthright reporting of the dangers of this method of anesthesia when incautiously administered. On the other hand, probably more frequently in discussion than in writing, one encounters in other sections quite arbitrary and dogmatic criticism of what is clearly becoming a valuable addition to the methods of anesthesia.

Having carried out short operations under intravenous Pentothal Sodium administered by the syringe method for several years, I and members of the Anesthesia Department at St. Vincent Hospital developed an interest in the use of Pentothal Sodium for major surgical procedures. The approach was based on a systematic attempt to combine intravenous Pentothal Sodium and regional nerve block in a complementary fashion, whereby each would compensate for the inadequacies and undesirable features of the other. After a year of work with this method, it has been brought to such a satisfactory state that in all age groups and in all general surgical cases, except the few enumerated below, it has become entirely the anesthesia of choice for major as well as minor surgical operations. The exceptions are operations in children under seven or eight years of age, because of the small caliber of the veins; operations about the neck, in the absence of intratracheal intubation, because of the too easy stimulation of reflex laryngospasm; operations on patients over sixty years of age who are to undergo a prolonged operative procedure, because of the unsatisfactory metabolic destruction of large doses of the drug and the danger of pulmonary edema from prolonged depression; operations on patients with vomiting, asthma or abdominal distention.

The degree to which combined intravenous Pentothal Sodium and local nerve block has become in our hands the anesthetic of choice for general surgery (excluding its orthopedic branch) is indicated by the selection of anesthesia for the last 784 cases operated on by me during the past year. Local anesthesia was used in 95 cases, spinal anesthesia in 96, inhalation anesthesia (nitrous oxide or cyclopropane or ether) in 80, Pentothal Sodium by syringe in 124 and continuous-drip Pentothal Sodium with local nerve block in 389 cases. Thus, intravenous Pentothal Sodium was

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the major anesthetic agent in 64 per cent of approximately 800 surgical cases of all types. The other agents were each used in about 10 per cent of the cases.

It is becoming generally recognized that intravenous Pentothal Sodium as the sole anesthetic agent does not provide adequate muscular relaxation in an acceptably high percentage of cases, unless used in an excessive quantity that encroaches on the danger zone of respiratory depression. This has led to a search for satisfactory combinations with other methods to provide a satisfactory and safe anesthesia. It is well recognized that supplemental administration of extremely small amounts of cyclopropane or ether quickly and completely takes up the deficiencies of Pentothal Sodium with respect to relaxation. Many surgeons have reported the supplemental use of nitrous oxide and oxygen with this drug, but in our hands it was not found to afford additional help at all comparable with the results procured by the complemental use of regional nerve block. In the few cases in which this combination failed to provide sufficient relaxation of the accessory muscles of respiration to permit easy closure of the peritoneum, nitrous oxide and oxygen did not produce an iota more of relaxation. The deficiency was quickly taken up by a small amount of cyclopropane or nitrous oxide and ether. This situation arose in only 3 or 4 per cent of the cases. No supplemental anesthesia was needed in the rest. Interrupted oxygen administration was carried out, however, when there was the least suggestion of cyanosis, in all cases of anemia, in all prolonged cases and in elderly patients who undoubtedly had some arteriosclerosis or myocardial changes.

Recent reports on the use of curare, a short-acting drug that paralyzes the myoneural junction of skeletal muscles, to produce relaxation is of interest, although its total systemic action indicates caution in its use until it has been thoroughly investigated.

In this series, Pentothal Sodium was administered in a 1 per cent solution by the continuous-drip method, which has been well described in the literature. In the infrequent cases in which the veins were so small as to cause an unsatisfactory rate of flow, a 2 per cent solution was used. After induction, the drug was administered during the period of maintenance in repeated and grouped subminimal fractions of either 5-cc. or 10-cc. amounts, depending on the rate of metabolic destruction of the drug in the given case. Between each subminimal fraction there was a wait of one minute to observe its effect on the respiratory center. The drug was given from the usual intravenous-infusion apparatus, with the drops regulated through a Murphy drip to about 250 drops per minute for induction and to about 130 to 140 per minute for maintenance. A companion infusion apparatus provided for continuous administration of saline or glucose solution during the intervals between the groups of Pentothal Sodium fractions, and for the instantaneous administration of plasma or blood without disturbing the patient during the operation. The intervals between fractions were five to fifteen minutes. Having observed the syringe technic for several years, we adopted the above method as the simplest, most dependable and most flexible way of administering Pentothal Sodium.

Local anesthesia — by 1 per cent novocain — was used to take up the deficiencies of the Pentothal Sodium. In the rare cases in which skin sensibility was of so high an order that it was not readily obliterated with the usual quantities of Pentothal Sodium, quick infiltration of the line of incision with novocain permitted this barrier to be easily passed. Relaxation of the rectus muscle comparable to that of spinal anesthesia was procured by direct block of the intercostal nerves in the rectus sheath. Patterns of blocking the sympathetic or intercostal nerves according to the type of operation were mapped out from the background of general experience with regional anesthesia.

In major abdominal operations, Pentothal Sodium alone was capable of controlling all reflexes arising from ordinary manipulations within the peritoneal cavity. Deep reflexes, however, which are elicited by traction on the viscera or their mesenteries, and whose control would have required deep planes of Pentothal Sodium anesthesia, were eliminated by blocking the sympathetic pathways with novocain. This was accomplished in the upper abdomen by anterior splanchnic block, in operations on the bowel by mesenteric block and in pelvic operations by block of the ganglions and sympathetic nerves involved.

This complemental use of the two agents provided a completely satisfactory anesthesia, comparable in all respects, and superior in many, to spinal or deep general anesthesia. It was accomplished with the administration of only moderate doses of Pentothal Sodium. If the two methods are effectively combined, the result provides a speedy, safe type of anesthesia, with an induction and recovery experience strikingly freer of unpleasant and uncomfortable episodes than is the case with the other principal anesthetic methods. Nausea and vomiting are infrequent; postoperative catheterization of male patients is rarely necessary, and in cases of herniorrhaphy has practically disappeared; postoperative headache does not occur; the administration of parenteral fluid, except as required by the technical exigencies of the operation, is reduced almost to the vanishing point; and early ambulation is favored.

Particular consideration should be given to the question of anterior splanchnic block. The method of choice for upper abdominal operations on the Continent, it has found but limited favor in America.

Finsterer and Thorek[3] and de Takats[4] in particular have used it in America. Combined with skillfully administered Pentothal Sodium anesthesia and rectus block, it constitutes an ideal anesthetic method for all operations on the stomach, spleen, gall bladder and ducts. The patient sleeps throughout the operation; there is complete flaccid paralysis of the rectus muscles; there is no reflex stimulation of the respiratory center from traction on the mesentery of the stomach or gall bladder; there is free delivery of the organs up into the incision; there is controllable respiratory quietude; there is never retching, nausea or vomiting; there is very rarely any drop in blood pressure; the pulse does not usually rise, and rarely passes 100; the patient can be maintained in an extremely light plane of Pentothal Sodium anesthesia; there is comfortable and not too delayed recovery from the anesthesia; and instantaneous operative support by the administration of plasma or blood is available as well as continuous saline or glucose infusion, without other disturbing manipulations. Little more can be asked to classify an anesthesia as nearly ideal.

In 1918, Kappis[5] first published detailed reports of 200 cases operated on under posterior splanchnic anesthesia by the paravertebral approach. In the same year, Wendling[6] suggested blind penetration of the unopened abdominal wall with a long needle at the level of the first lumbar vertebra to produce splanchnic anesthesia, but of course such a suggestion was never seriously considered. In 1919, Braun[7] reported the use of anterior splanchnic block by way of the opened abdomen. Finsterer has been an ardent advocate and practitioner of the method, as have been many German surgeons. In 1926 he and Thorek[3] reported 2373 cases collected from the literature and personal communications from several German surgeons without a single anesthetic fatality; they were unable to find a single death from this method up to 1936.

The use of splanchnic anesthesia in this series has controlled the strong reflex stimulation of the respiratory center from traction on the subdiaphragmatic mesenteries, the activation of which leads to a high rate of utilization of Pentothal Sodium. During anesthesia from this drug alone these deep powerful reflexes make surgery difficult as a result of extreme activation of the muscles of respiration, particularly the lateral abdominal muscle and the diaphragm. Large doses of Pentothal Sodium administered to suppress this forced breathing activity encroached on the zone of respiratory depression to such an extent that in a few cases transient apnea was encountered. Splanchnic anesthesia controls these undesirable restrictions on the use of Pentothal Sodium, and provides abdominal quietude, adequate relaxation of the accessory muscles involved in the stimulated breathing and minimal excursions of the diaphragm. These effects result in a reduction of about 1 gm. in the average total dosage of Pentothal Sodium required. This is illustrated by two series of cholecystectomies, each comprising 22 cases. In the first series, in which Pentothal Sodium and rectus block were used, the average dose of the drug was 2.19 gm.; in the second series, in which splanchnic block was added, the average dose was 1.23 gm.

It will be appropriate to report a modified technic for anterior splanchnic block, based on a special splanchnic needle guide that I devised (Fig. 1).

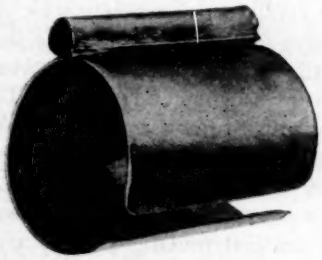

FIGURE 1. *Splanchnic Needle Guide.*

The modification and the guide convert a moderately difficult technical procedure, particularly in the obese abdomen, into a relatively simple and safe procedure. With this modification the procedure was carried out with ease in a deep-chested, obese patient weighing 235 pounds. The purpose of anterior splanchnic block is to deposit an anesthetizing dose of novocain retroperitoneally at the level of the first and second lumbar vertebras between the aorta and the inferior vena cava. This is an isthmic point or meeting place for all sympathetic nerves and plexuses deriving from the greater and lesser splanchnic nerves and the sympathetic trunks, which supply the stomach, duodenum, pancreas and transverse colon. In the usual technic the finger is pressed downward above the lesser curvature of the stomach and cephalad to the upper border of the pancreas as well as the celiac axis, until it encounters the body of the first lumbar vertebra. In so doing it carries the lesser omentum in the hilus region of the liver down under it, so that resistance and intervening vague fatty tissues confuse the certainty with which the tip of the finger contacts the vertebra and keeps free from underlying structures. The aorta is identified on the right side of the fingertip, and by pressing the aorta to the patient's left and pressing firmly on the vertebral body, the aorta is safely separated from the inferior vena cava. The novocain needle is then inserted directly over the tip of the finger until it distinctly contacts the body of the first lumbar vertebra, when the novocain is injected. The technic may be decidedly difficult in an extremely or even a moderately obese patient. There is a distinctly blind aspect to this technic.

My modified technic makes the procedure certain, safe, easy and exact. With the patient satisfactorily

anesthetized with Pentothal Sodium, two broad-bladed retractors are placed under the left and the adjacent portion of the right lobe of the liver, retracting them upward. A pack is placed along the lesser curvature and over the anterior surface of the stomach so that the left hand can retract it downward, tensing the lesser omentum, particularly where it enters the hilus of the liver. Lateral pressure to the patient's left by the index finger over the corner of the pack carries the fundus of the stomach outward and improves exposure. About in the midline the caudate lobe of the liver is nearly always identified behind the lesser omentum, where the omentum passes between the left lobe of the liver and the caudate lobe. The caudate lobe has a purplish-brown appearance behind the thin screen of the omentum. With the omentum still tensed by downward traction of the left hand, a vertical rent is established in this avascular lesser omentum by an instrument, directly over the tip of the caudate lobe. This permits the caudate lobe to move forward into the rent so that its tip presents in front of the omentum. Usually this area is free of fat and completely avascular, although an occasional vessel may traverse the area. In extremely thin persons nothing is gained by opening the omentum. The tip of the middle finger of the left hand is then advanced cautiously through the rent into the lesser omental bursa, until it comes into direct contact with the body of the first lumbar vertebra. There are now no obscuring membranes between the finger tip and the bone. The pulsating aorta is identified above the celiac artery and the upper border of the pancreas.

The finger and hand are then withdrawn. The splanchnic needle guide is fitted over the second and third phalanges of the middle finger of the left hand. The left hand is again placed in its previous position of retraction over the stomach, again advancing the middle finger, this time bearing the splanchnic needle guide, under the caudate lobe and into the lesser omental cavity, until it again contacts the first lumbar vertebra as a distinct bony structure with no intervening membranes. Pressure firmly applied to the patient's left against the pulsing aorta and downward against the bone safely separates the aorta from the inferior vena cava. A strong 15-cm. 18-gauge needle, attached to a novocain syringe, is inserted in the proximal opening of the small needle guide, through which it is easily and accurately advanced until it impinges abruptly and definitely on the first lumbar vertebra, directly over the tip of the nail of the middle finger, and separated from it by a few millimeters. If desired, the splanchnic guide may be slightly rotated so that the needle can advance a fraction to the right or the left of the middle of the finger tip, according to the dictates of the underlying anatomy of the aorta.

When firm contact by the needle point against the body of the vertebra has been established, 20 cc. of a 0.5 per cent novocain solution is injected. During a long operation 10 cc. may be repeated hourly. Almost immediately respiratory quietude and relaxation pervade the whole subdiaphragmatic region, with complete obliteration of the disturbing reflex stimulation of respiration previously evoked by traction on the upper abdominal viscera or their mesenteries.

Summary

A brief preliminary report is presented concerning a satisfactory experience during the past year in using intravenous Pentothal Sodium anesthesia with regional nerve block for major surgical procedures in a complemental fashion.

A modified technic for anterior splanchnic block anesthesia, based on the use of a needle guide improvised for accurately carrying the splanchnic needle to assured and safe contact with the first lumbar vertebra, is presented.

Following rather extensive experience with this method, a search was made in the literature for the report of a device like the above-described splanchnic needle guide. Only one brief note was found. Burke[8] used the same basic principle. He attached a flexible ring to the end of a long grooved director and used the director to guide the splanchnic needle.

References

1. Editorial. Local versus general anaesthesia. *Lancet* **1**:802, 1922.
2. Gorth, W. L. Some observations of anesthesia abroad. *Anesth. & Analg.* **17**:292-297, 1938.
3. Finsterer, H., and Thorek, P. Splanchnic anesthesia: its importance in operations of upper abdomen. *Am. J. Surg.* **25**:481-486, 1934.
4. de Takats, G. Splanchnic anesthesia: critical review of theory and practice of this method. *Surg., Gynec. & Obst.* **44**:501-519, 1927.
5. Kappis. Cited by de Takats.[4]
6. Wendling. Cited by de Takats.[4]
7. Braun, H. *Local Anesthesia.* Translated and edited by M. L. Harris. Philadelphia: Lea & Febiger, 1924.
8. Burke, J. New instrument in splanchnic anesthesia. *J. A. M. A.* **82**: 790, 1924.

DEATH FROM SULFADIAZINE WITH AGRANULOCYTOSIS, JAUNDICE AND HEPATOSIS

Report of a Case

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THE occurrence of various types of toxic reactions to the sulfonamides is now common knowledge, and all have been fully described in the medical literature[1–5] in recent years. There have been reported a sufficient number of severe reactions producing death to make the medical profession fully conscious of this danger and of its obligations in this respect. Reactions from the newer compounds have been fewer than those from the older ones. Thus, those seen following the use of sulfathiazole are much less frequent than are those from sulfanilamide, and those resulting from sulfadiazine appear to be still fewer in number. Although agranulocytosis and focal necrosis of the liver have been seen as manifestations of toxicity due to sulfathiazole administration, we, who are not in a position to make a thorough search of the current literature, are not familiar with any report of agranulocytosis and liver damage following the use of sulfadiazine. Simon[1] in a comprehensive review of the pathologic lesions seen in both animals and man states that the most extensive and widespread types of focal necrosis of the liver are seen in deaths following sulfathiazole therapy, but does not mention similar lesions resulting from sulfadiazine. The following case of death after sulfadiazine administration is cited as one believed to have resulted from agranulocytosis and jaundice, in which there was a diffuse hepatosis of moderate degree and marked congestion and early central necrosis of the liver.

CASE REPORT

The patient, a 23-year-old man, had been ill with abdominal pain for 72 hours prior to admission to a regional station hospital of the Army Air Force in Florida. He had previously been in good health and could recall no previous illnesses of any account. He was closely questioned regarding any previous administration of the sulfonamide drugs and was positive that none had ever been given. The history was typical of acute appendicitis, with generalized abdominal pain that had persisted for 24 hours, followed by pain in the right lower quadrant for 48 hours. It was unaccompanied by nausea, vomiting, chills, fever or urinary complaints, and there had been no bowel movement for 3 days.

Examination of the abdomen on admission revealed it to be flat and without distention, muscle spasm or the presence of a mass. Localized tenderness was present in the right iliac fossa, but rectal examination revealed no tenderness or induration. The white-cell count was 10,250, the pulse 100, and the temperature 101.2°F. The policy in this hospital was not to subject any patient to operation for appendectomy if it was thought that perforation of the appendix had occurred but rather to treat such cases conservatively. This case, however, did not suggest perforation, and the patient was operated on under spinal anesthesia within a few hours of admission. When the peritoneum was opened through a McBurney incision, foul-smelling, cloudy fluid was encountered, from which a paracolon bacillus was cultured. The appendix was adherent to the cecum, the wall of which was markedly indurated. Inasmuch as attempted removal of the appendix would have been extremely difficult, the operation was concluded by placing 10 gm. of sulfanilamide in the peritoneal cavity in the region of the appendix and closing the wound in layers around a cigarette drain.

Postoperative treatment consisted of constant Wangensteen suction, supportive therapy with adequate fluid intake intravenously, morphine, nothing by mouth and 5 gm. of sodium sulfadiazine administered in two doses daily by the intravenous route (Fig. 1). The course was somewhat stormy for 9 days, during which time the temperature fluctuated in the neighborhood of 102°F. and the pulse around 100 per minute. Considerable distention developed in spite of the continuous gastric suction, and on the 8th postoperative day this had reached such proportions that it was thought advisable to pass a Miller–Abbott tube. This was successfully passed into the duodenum, whence it rapidly traveled to the lower ileum and decompressed the abdomen completely within 12 hours. The temperature was normal on the 9th day, intestinal suction being discontinued on the 12th day. Intravenous sulfadiazine was discontinued on the 11th postoperative day, and thereafter was given in 2-gm. daily doses by mouth until the 18th day.

During this entire interval the blood chemical findings and cell counts were satisfactory, and although the wound continued to discharge a moderate amount of pus, the patient appeared to be making a satisfactory recovery after the 12th day.

On the 16th postoperative day, the temperature reached 100°F., and increased daily so that by the 21st day it had reached 104. The distention did not recur, and repeated examinations of the abdomen and rectum revealed no evidence of a recurrence of abscess formation. Fluoroscopic and x-ray studies of the diaphragm and chest were normal. Two days after the onset of this fever the daily 2-gm. dose of sulfadiazine was discontinued in the belief that this might have accounted for the febrile reaction, but the temperature continued to rise for 4 more days. The white-cell count which was 9000 when the drug was discontinued, dropped to 4000 on the following day, but rose to 5900 on the 21st day. The possibility of pylephlebitis and multiple liver abscesses as a cause for the fever was entertained, but there was no evidence of icterus or ascites of even mild degree. On the 22nd day of the illness, it was believed that there was some increased induration in the region of the wound that might possibly account for the recurrence of fever, and a second operation was therefore undertaken.

Under intravenous Pentothal Sodium anesthesia the original wound was explored with the finger. Although it was unhealthy in appearance, no abscess pockets were encountered, and the operation was concluded in 10 minutes. While the patient was on the operating table there again was considerable discussion by members of the staff concerning the cause of the fever. Pylephlebitis with multiple liver abscesses was again considered. Several medical officers inspected the scleras in a good light for evidence of an early jaundice, but none was seen.

Within 2 hours after the operation several dramatic incidents occurred. First, the patient developed cyanosis, which was rapidly and successfully treated with oxygen and intravenous caffein sodium benzoate. During this time he was receiving 2.5 gm. of sodium sulfadiazine intravenously. Within 1 hour marked jaundice suddenly developed, and blood studies revealed an icteric index of 106 (van den Bergh, 38 mg. per 100 cc.), and the startling fact that the white-cell count had dropped to 450. Blood smears at that time revealed a total absence of granulocytes. These untoward developments were accompanied by a rise in temperature to 106°F. and an increase in the pulse to 130.

For the next 5 days, the condition of the patient was critical, with the temperature fluctuating between 104 and 106°F. and the pulse between 130 and 160. The jaundice increased,

the icteric index reaching 177 on the 3rd postoperative day. Although the serum protein level was above 6 gm. per 100 cc., the albumin-globulin ratio dropped to 1.1. All the other blood findings, including the nonprotein nitrogen, blood phosphatase, chloride, hemoglobin and red-cell count, remained within normal limits. General supportive measures were undertaken, including the adequate administration of fluids, continuous oxygen and transfusion of 1000 cc. of fresh compatible citrated blood daily. These procedures were of no avail, although the white-cell count did rise to 2450 and 2000 on the 3rd and 4th postoperative days. The smears, however, continued to show an absence of granulocytes in the blood, and the patient expired on the 5th day after the second operation, 26 days after admission.

Autopsy. Autopsy was started within 1 hour after death. The body showed evidence of considerable weight loss. The skin and conjunctivas were markedly icteric. Two cigarette drains were present in the recent McBurney's incision, along which was noted a small amount of foul-smelling, purulent-looking material. The greater omentum was pulled to the right and was held by thick fibrinous adhesions to the peritoneal lining of the right lower quadrant of the abdomen, thus walling off this area. The peritoneal cavity was otherwise unaffected except for approximately 5 cc. of purulent-looking material walled off by thick fibrinous adhesions in the rectovesical space. The distal half of the appendix had been eaten away, and the wall of the stump was slightly thickened, and its serosa granular and reddened. The small tributaries of the superior mesenteric vein draining the terminal ileum, cecum and appendix were cross-sectioned approximately every centimeter of their distance and found to be patent, as were the arteries. The superior mesenteric and portal veins were opened throughout their length, but no thrombi or break in the intimal lining was observed. The regional lymph nodes were markedly enlarged, grayish yellow and fairly firm in consistence.

The lower edge of the liver was 1 fingerbreadth below the right costal margin, the left lobe extending to the left anterior axillary line. The common bile duct and the hepatic duct and its large branches were opened upward from the ampulla of Vater, but no obstruction or stone was noted. The cystic duct showed no abnormalities. The wall of the gall bladder was not thickened and contained no stones. On section of the liver the edges everted markedly. The liver was reddish brown and on close inspection had a nutmeg appearance. The entire liver was sectioned into thin slices and presented the same picture throughout. The consistence of the organ was not changed to any appreciable extent.

The spleen was dark reddish blue and approximately three times its normal size. It was firm and retained its shape on removal from the body. The mucosa of the cecum was reddened, granular and swollen. The kidneys were swollen and the edges everted on section. The cortex of each kidney was pasty yellow and was moderately widened. The medullas were injected. The capsules stripped with ease, leaving smooth, even surfaces. The suprarenal glands were of normal size but were slightly softer than normal.

The lungs showed no abnormalities other than for congestion and edema in the most dependent portions. The pleural cavities were free of adhesions. The pericardial cavity contained approximately 50 cc. of bile-stained watery fluid. The pericardial lining was smooth and glistening throughout. The heart was flabby and did not retain its shape on removal from the body, the musculature being brownish red and soft. The coronary vessels were patent throughout, and the valves were not thickened. The intima of the first part of the aorta contained an occasional atheromatous plaque. The lining of the aorta had a yellowish tint, as did many other tissues throughout the body.

The bone marrow of the sternum and ribs was hypoplastic. Smears from sternal bone marrow showed a hyperplasia of immature myeloid elements with an apparent arrest of matura-

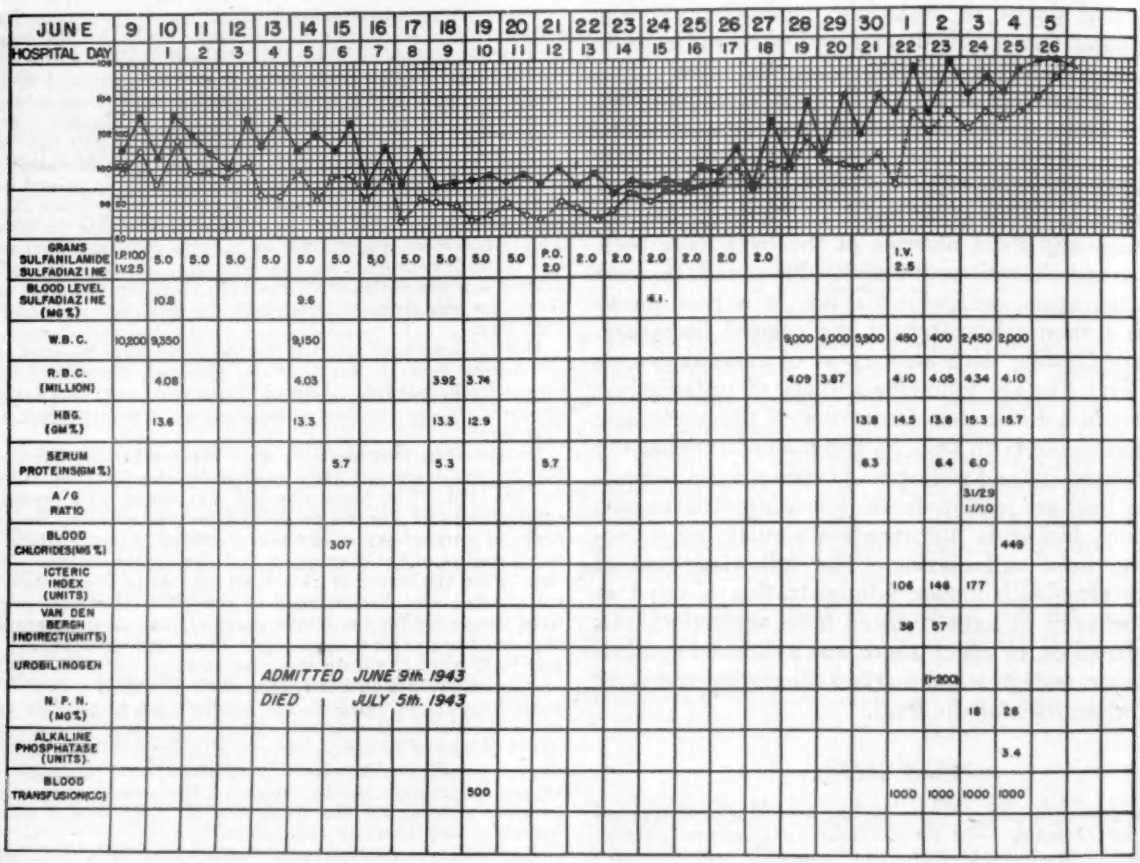
JUNE 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 1 2 3 4 5
HOSPITAL DAY 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26
GRAMS SULFANILAMIDE SULFADIAZINE
BLOOD LEVEL SULFADIAZINE (MG%)
W.B.C.
R.B.C. (MILLION)
HBG. (GM%)
SERUM PROTEINS(GM%)
A/G RATIO
BLOOD CHLORIDES(MG%)
ICTERIC INDEX (UNITS)
VAN DEN BERGH INDIRECT(UNITS)
UROBILINOGEN
N.P.N. (MG%)
ALKALINE PHOSPHATASE (UNITS)
BLOOD TRANSFUSION(C.C.)
ADMITTED JUNE 9th. 1943
DIED JULY 5th. 1943

FIGURE 1.

tion at the myeloblastic level. Most of the cells appeared to be myeloblasts, containing from two to three nucleoli.*

Microscopical study of the tissue revealed less damage to the liver cells than had been expected from the deep jaundice. The central veins were engorged, with resulting atrophy and early focal necrosis of the adjacent liver cells. Fat stains revealed focal areas of fatty degeneration of the liver cells, which were more marked in the central areas. The remainder of the liver cells showed swelling, increased granularity and bile retention, but otherwise they were fairly well preserved. Study of many sections failed to reveal any evidence of obstructive dilatation of the intrahepatic bile ducts, which substantiated the autopsy finding of no obstruction of the large bile ducts. There was no histologic evidence of previous liver damage (this is often present in persons showing liver disease from sulfonamide drugs).

The appendix showed a subserosal zone of necrosis with bacterial colonization and with practically no cellular reaction. The reaction of the mesentery to the peritonitis was practically exclusively plasmocytic and lymphocytic, with an interspersion of an occasional macrophage and histiocyte. If only sections showing the reaction to the peritonitis had been seen, one would of necessity have considered seriously the rare entity of aleukemic plasma-cell leukemia.

Microscopical examination of the spleen revealed marked depletion of nucleated elements of both follicles and pulp. The kidneys showed normal glomeruli and cloudy swelling of the tubules. Many bile casts and an occasional hemoglobin cast were found.

A blood culture taken at the time of the post-mortem examination and grown on tryptose phosphate broth and heart-infusion broth showed a gram-positive rod, a gram-negative rod and a gram-positive coccus. This finding had little significance, since blood cultures taken a few days after the second operation and planted on the same mediums were still sterile after 21 days of incubation.

The points to be stressed in the progress of this patient are as follows. Up to the sixteenth postoperative day he was apparently making a satisfactory recovery from incision and drainage of a local peritonitis due to perforation of the appendix. Fever then recurred to an increasing degree daily, and four days after sulfadiazine therapy was discontinued the fever continued to rise, reaching a maximum of 104°F. Following the second operation a short period of anoxia occurred during the administration of 2.5 gm. of sodium sulfadiazine intravenously. Sudden and rapid onset of jaundice, accompanied by a marked leukopenia and agranulocytosis, occurred within one hour of administration of the sulfadiazine. Lastly, post-mortem examination showed no evidence of infection to account for the fatal termination, but did reveal a hyperplasia of immature myeloid elements, with an apparent arrest of maturation at the myeloblastic level in the bone marrow, and enlargement of the liver due to a diffuse hepatosis with early central focal necrosis. Histologic examination of the liver failed to give a completely satisfactory explanation for the intense jaundice.

In retrospect it is believed that the febrile reaction occurring from the sixteenth to the twenty-second postoperative day was a toxic reaction to sulfadiazine, the patient having received 71.5 gm. of the drug up to the eighteenth day. It is further considered that the sudden development of jaundice and agranulocytosis after a further administration of 2.5 gm. of sulfadiazine probably produced an exacerbation of the hypersensitiveness to sulfadiazine, with the resultant liver and bone-marrow changes that led to the fatal outcome.

*All these findings were confirmed by Dr. Roy R. Kracke, of Emory University.

Summary

A fatal case following the administration of sulfadiazine and presumably due to toxic damage of the liver and bone marrow is described, and the post-mortem findings are discussed.

References

1. Simon, M. A. Pathologic lesions following administration of sulfonamide drugs. *Am. J. M. Sc.* **205**:439-454, 1943.
2. Richards, V. Sulfonamides in surgery. *Surgery* **14**:308-319, 1943.
3. Sutliff, W. D., Helpern, M., Griffin, G., and Brown, H. Sulfonamide toxicity as cause of death in New York City in 1941. *J. A. M. A.* **121**:307-313, 1943.
4. Dowling, H. F., and Lepper, M. H. Toxic reactions following therapy with sulfapyridine, sulfathiazole and sulfadiazine. *J. A. M. A.* **121**: 1190-1194, 1943.
5. Johnson, S. A. M. Acute agranulocytosis due to administration of succincylsulfathiazole. *J. A. M. A.* **122**:668, 1943.

TUMOR OF THE CAROTID BODY*

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THERE is nothing new to be said in regard to tumors of the carotid body. The only excuse for presenting this subject to the surgical profession is a plea for a correct preoperative diagnosis. If this is made, it may well be possible to reduce the rather high mortality that has accompanied the surgical cure of this lesion.

The correct diagnosis should not be too difficult provided that one considers carotid-body tumor in the differential diagnosis. The only difficulty has been that this condition is not frequently encountered, and that therefore one fails to give it consideration.

The carotid body was first mentioned by von Haller[1] in 1743, and was described in detail in 1862 by Luschka.[2] It is a tiny organ about the size of a grain of rice situated at or near the bifurcation of each common carotid artery. It is supposed to reach full development at about the age of twenty, but in some cases it either does not exist or is so tiny that it is not found at autopsy. It is always closely attached to the wall of the carotid artery, but its exact location is not constant.

Embryologically the carotid body is a complex structure of somewhat disputed origin. By some it is supposed to arise from mesodermal tissue of the third branchial cleft and to be somewhat homologous to the medullary portion of the suprarenal gland. By others it is thought to have its origin in the sympathetic nervous system. Certainly it is well supplied with nerve fibers. It is intimately associated with the periarterial sympathetic fibers of the carotid artery, receives fibers from the glossopharyngeal nerve and the upper cervical sympathetic ganglion, and sometimes has a communicating branch with the vagus nerve.

Physiologically it is apparently of no great importance. There is little or no evidence in favor of including it among the glands of internal secretion. The facts that it is sometimes absent and that bilateral extirpation can be carried out without any subsequent symptoms suggest that its function, whatever it may be, is negligible. This being so, the only clinical interest in the carotid body is its pathology, and the only pathologic lesion is a tumor. It is said that the first recorded operation for tumor of the carotid body in America was performed by Middleton[3] in 1895. The tumors in general maintain the same histologic characteristics as does the normal carotid body. Definite malignancy as indicated by active mitosis is found in 50 per cent of the tumors, and all are potentially malignant. Distant metastasis has never been proved, but local recurrence has occurred in 20 per cent of the malignant cases.

The tumors are usually unilateral, but an occasional bilateral involvement has been reported. They manifest themselves as painless, slow-growing tumors situated in the superoanterior cervical triangle, pushing out from under the anterior border of the sternomastoid muscle. They are usually ovoid, firm but elastic and deep seated, and are never attached to the skin. They are extremely vascular. Sometimes a bruit or thrill is present, and often a transmitted pulsation from the carotid arteries is evident, but this is to be differentiated from the expansile pulsation of an aneurysm. Compression of the carotid artery below the tumor abolishes the bruit, thrill or pulsation and sometimes causes a diminution in its size. These tumors usually have some lateral mobility, but possess little or no vertical mobility because of their firm attachment to the carotid artery. This is an important diagnostic point.

Carotid-body tumor is a disease of middle age, the average age of patients being about forty-five years at the time of operation, but some of the tumors have been present from ten to fifteen years, with an average duration of five or six years.

When any other symptoms, aside from slow, painless growth, are present, they are usually caused by invasion or compression of other important regional structures, such as the vagus nerve, the sympathetic or recurrent laryngeal nerves or the pharynx or esophagus. Episodes of fainting, hoarseness, dyspnea, dysphagia, cough, tinnitus or headache have been reported, as has Horner's syndrome from pressure on the cervical sympathetic nerves.

The correct diagnosis of these tumors is rarely made preoperatively — in less than 10 per cent of the reported cases. This is undoubtedly due to the fact that the condition is so rare that its existence is not even considered by the examining physician. Only 20 cases of carotid-body tumor were to be found in the records of the Mayo Clinic in 1941, and somewhat over 200 in the entire medical literature.[4] The most frequent incorrect diagnoses are tuberculous adenitis, branchial cyst, metastatic carcinoma, aberrant thyroid gland and aneurysm.

If the diagnosis of carotid-body tumor is considered at all, it should not be too difficult to arrive at the correct answer. The most important indica-

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tion of such a diagnosis is the presence of a slowly growing, painless, deep-seated tumor in the upper anterior neck, particularly if, as before mentioned, there is lateral mobility without vertical mobility, not to mention marked transmitted pulsation, and perhaps diminution in the size of tumor on cutting off the circulation by pressure on the common carotid artery.

The importance of establishing the correct diagnosis before operation is that steps can then be taken to reduce the dangers involved by the operative procedure. The chief danger is death from cerebral anemia or hemiplegia, should sacrifice of the carotid arteries be necessary at the time of excision.

It is generally accepted that surgical removal is the ideal treatment for tumors of the carotid body, particularly if this can be done without sacrifice of the carotid vessels. Some years ago, however, Bevan[5] expressed the opinion that if the tumor proved to be inoperable without sacrifice of these vessels, the incision should be closed as would be done in any other exploration for inoperable disease, and the patient treated with radium or x-rays. Little is found in the literature, however, to indicate that these tumors can be treated successfully with radiation. There is also some doubt whether it would be possible to go no farther after exploring the tumor sufficiently to determine that the carotid vessels must be sacrificed. At such a point one might well be committed to a completion of the operation to control the bleeding from the extremely vascular tumor. A complete removal of the tumor is indicated even at the additional risk involved because of its malignant or potentially malignant nature.

In a series of 159 cases reviewed by Phelps, Case, and Snyder[6] in 1937, the mortality rate was 24 per cent. In the series of 20 cases at the Mayo Clinic, reported by Harrington, Clagett and Dockerty[4] in 1941, the mortality was 20 per cent; in the cases in which ligation of the carotid vessels was necessary it was 44 per cent. The average age of the patients who died following ligation was fifty-three, and that of those who survived it was thirty-one. This indicates an increasing risk with advancing age.

Because of this pronounced danger, particularly in old patients, it seems wise to give every possible preoperative preparation to the patient in whom a tumor of the carotid body is suspected. This preparation should consist of systematic compression of the common carotid artery against the transverse process of the sixth cervical vertebra. This pressure should be carried out for an increasing duration of time, and several times a day, over a period of several weeks if necessary, until the patient can tolerate complete compression of the vessel for long periods without experiencing faintness or loss of consciousness. Linton[7] has developed a tourniquet in the form of a rigid collar around the neck; pressure is exerted on the carotid artery by means of a pad activated by a screw. It is hoped by this procedure that the collateral circulation to the brain on the affected side can be improved.

There is some difference of opinion whether collateral circulation in this part of the body can be developed. Possibly in certain cases anatomic variation in the arterial circulation at the base of the brain may prove to be an unsurmountable barrier. Certainly if a patient has a so-called "carotid reflex," — namely, syncope caused by pressure on the carotid artery, — one should hesitate to divide the artery at operation unless the reflex can be abolished by some such development of collateral circulation as is suggested above.

There are of course other structures that may be injured during the operative removal of a carotid-body tumor. Some of these are the internal jugular vein, the vagus nerve, the recurrent laryngeal nerve, the hypoglossal nerve and the cervical sympathetic chain. With care and a proper technic, however, these injuries should be reduced to a minimum, and naturally they are not so serious as a hemiplegia.

The clinical case that brought this subject again to my attention is as follows.

Case Report

M. H., a 44-year-old, unmarried woman, consulted me on January 18, 1944, because of an unsightly swelling in the right side of her neck. She had first noticed a small lump in this area in 1935. This had gradually increased in size. She had had no pain or discomfort, except for occasional attacks of headache.

Examination revealed a tumor in the upper neck, just anterior to the sternomastoid muscle, 7 cm. in diameter with the vertical dimension slightly longer than the horizontal. It was firm and nontender. There was a definite bruit and pulsation that seemed to come from surrounding vessels and not from the tumor itself. The latter was slightly movable in a lateral direction. There was a vertical scar 5 cm. long over the tumor where a surgeon had attempted several years previously to remove it, but had stopped the operation, explaining to the patient that he was not prepared for such a serious dissection as would be necessary for its removal. I believed that this tumor probably arose from aberrant thyroid tissue and advised operation.

Operation was done under a general anesthesia. Owing to the extreme vascularity of the tumor, every precaution was made to control all small blood vessels, and the dissection was carried out slowly and carefully through an ample incision. The tumor was eventually entirely exposed and seemed to arise from the bifurcation of the carotid artery. It could be dissected from the carotid, however, without damage to that vessel, and the wound was closed. The patient made a comfortable, uneventful recovery, being discharged from the hospital in 4 days. The pathologist reported a tumor of the carotid body, which had not been considered as a possible diagnosis.

Summary

Tumors of the carotid body are rare, but should be considered in all slowly growing, painless tumors of the upper neck, and if considered, the correct diagnosis should be arrived at with reasonable accuracy. Their incidence is the same in both sexes. The majority of patients are between forty and sixty years of age.

These tumors are always either malignant or potentially so. They rarely recur, and almost never metastasize after complete surgical removal.

The operation is delicate and dangerous.

Ligation of the carotid vessels is necessary for complete removal in 50 per cent of the cases.

Preoperative preparation consists of systematic compression of the common carotid artery several times daily for gradually increasing periods until the patient can tolerate complete compression for long periods without syncope.

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References

1. von Haller. Cited by Bevan and McCarthy.[5]
2. Luschka, H. Ueber die drüsenartige Natur des sogenannten Ganglion intercaroticum. *Arch. f. Anat., Physiol. u. wissensch. Med.* 405-414, 1862.
3. Middleton, W. D. Some curiosities in surgical pathology. *Tr. Iowa State M. Soc.* **15**:91-98, 1897.
4. Harrington, S. W., Clagett, O. T., and Dockerty, M. B. Tumors of carotid body: clinical and pathological considerations of twenty tumors affecting nineteen patients (one bilateral). *Ann. Surg.* **114**:820-833, 1941.
5. Bevan, A. D., and McCarthy, E. R. Tumors of carotid body. *Surg., Gynec. & Obst.* **49**:764-779, 1929.
6. Phelps, F. W., Case, S. W., and Snyder, G. A. C. Primary tumors of carotid body: review of 159 histologically verified cases: report of case. *West. J. Surg.* **45**:42-46, 1937.
7. Linton, R. Unpublished data.

MEDICAL PROGRESS

PSYCHIATRY: REHABILITATION

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CURRENT psychiatric literature continues to be composed, in great part, of papers dealing with the psychiatric casualties of war. It is now well established that the earlier treatment is begun the better are the chances for recovery. Of course the same principle applies, and always has applied, to the psychiatric illnesses of peacetime living. So much has been written, both in scientific journals and in the popular press, about war nerves, combat fatigue or psychoneurosis that not only the public but psychiatrists themselves may have lost a well balanced perspective on this subject. Also popular alarm has been augmented by the large number of inductees rejected as "not suited for military service" on the basis of a neuropsychiatric or personality disorder.

Although exact statistics are not available, it is reported[1,2] fairly consistently that about 45 per cent of the medical discharges from the armed forces are for neuropsychiatric disability. Considering that the men receiving medical discharges to date constitute a small proportion of the grand total of those in service, the problem of the veteran who returns to civilian life with war nerves is not, and will not be, so appalling in extent as the alarmists portray. If qualities of human nature can be spoken of in the sense that human nature is at all responsible for them, it is a compliment to human psychobiologic integration that comparatively so few men become psychiatric casualties under the impact of the terrific conditions of combat.

There is, of course, the problem of rehabilitation for many men who develop nervous disorders during their time in service. Pratt[3] states that as of September, 1944, more than 300,000 men had been discharged for psychiatric conditions. Important considerations in this problem are insufficient facilities for treatment and the reluctance or refusal of numerous men to accept treatment. Even before the war, federal veterans' hospitals were overcrowded and there were less than 3000 psychiatrists in the country.[3] It may be hoped that the awareness of and interest in nervous or emotional disorders increased and, in many instances, awakened by the present war will be maintained, both by physicians who are not psychiatrists and by laymen.

The aversion of the veteran to seeking psychiatric treatment is not difficult to comprehend. Society has looked askance at psychiatry for generations. Gregg[4] refers to "the inherent, the inveterate, the inevitable handicaps of psychiatry." He writes, "The three most powerful traditions or historical heritages of psychiatry are still, as they have been from time immemorial, the horror which mental disease inspires, the power and subtlety with which psychiatric symptoms influence human relations, and the tendency of man to think of spirit as not only separable but already separate from body." Another handicap might be included. Neurotic and, to some extent, psychotic illness entails the question of personal responsibility, free will. Again and again the patient ill with neurotic symptoms expresses the wish that some physical cause might be found to explain his disability. At least half-consciously he fears to hear what he partly senses may be true, "It's up to you." Human pride or egotistic desire is such that it is difficult to admit that what is up to one may be more easily accomplished if one permits the doctor to help.

Government facilities for treating the veteran have not been, are not now and will not be adequate. It is well known that the veterans' hospitals have not been able to give satisfactory care and treatment to the casualties of World War I. Suggestions are

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being made that the federal government could contract for the care of veterans with the general hospitals. Cunningham[5] writes, "Veterans are best treated in community facilities," thus precluding bureaucratic organization. Terhune[6] states:

> This problem is too big for the government to handle. . . . If the government tries to care for these patients, after discharge from the Army, . . . results will be unsatisfactory. The practice of medicine is based on an individual relationship existing between doctor and patient — this necessary personal emotional transference cannot exist between a government bureau and patient. Therefore, it will be the job of civilian physicians, who know these men and are familiar with the facilities of the communities in which they live, to readjust them to civilian life.

Various writers have commented on the fact that the development of a nervous disorder under the circumstances of military service does not warrant the assumption that the man affected will be unsuited for at least a reasonably adequate adjustment to civilian pursuits. Burlingame,[7] in writing on industrial psychiatry, says:

> If a person is discharged from the armed forces with the diagnosis of psychoneurotic, it simply means that the individual did not have the necessary adaptability to become a successful employee of the armed forces. This diagnosis carries with it no adverse implication concerning that person's re-employability in industry.

It is to be remembered that over a million men have been rejected in this country as not fit for service in the armed forces because of some neuropsychiatric disability. Again, exact statistics are not available, but it is known that the majority of these men were carrying on successfully enough in civilian life.

If there is a correct understanding on the part of doctors and the public in general, most of the veterans who are nervous will readjust to life out of the service without great difficulty. Referring to the physician's treatment of the man who has not qualified for service, Terhune[6] writes:

> Explain that they were not rejected, they were just not accepted for military duty; that this was for their own protection, and because they could be more useful to the Nation in other lines of endeavor. Reassure them about their own essential fitness for civilian life, pointing out that many of the qualities which make for a successful civilian do not necessarily make for a good soldier.

If there exists, as part of man's response to his environment, a normal emotional reaction, — and outside of the psychiatrist's world, at least, it does exist, — then many of the fear and anxiety reactions engendered and precipitated by the indescribable conditions in combat zones cannot justifiably be labeled "psychoneurotic."

Thomas[8] refers to the injustice of calling all manifestations of fear, anxiety and depression psychoneurotic. In reporting on 4 cases in which there was temporary maladjustment, he writes:

> They constitute a behavior pattern that has been witnessed in armies throughout the ages. Until the advent of modern psychiatry, such conduct was attributed to a variation in men's capacity to sever themselves from their usual way of life and to conquer a fear of impending death. The will to fight, morale, training, fatigue, disheartening reverses and leadership were recognized as factors able to influence a man's emotions. These factors are acknowledged in this war, but the frequency with which the diagnosis of a psychoneurosis is made raises a suspicion that psychiatrists have encouraged a shrouding of them in an ill use of terminology. In doing so they have thrown the problem of psychoneurosis out of focus with what seem to be the facts. . . . There are psychiatrists who regard the familiar fear of a soldier in a dangerous situation as a measure of the emotion of an anxiety neurosis. This is tantamount to calling all frightened and bewildered soldiers psychoneurotic. . . . Careless use of the term ["anxiety"] does injustice to the Army, the soldier and the taxpayer.

Thomas suggests the use of the term "simple adult maladjustment" when the ramifications of what a diagnosis of psychoneurosis implies are not present. He continues:

> It is obvious from what has been said that I believe that some of these cases present problems in morale, discipline and stamina. If this is so, it follows that any term connoting a mental disorder will cloud the issue. The answer to the question seems to rest in the prophylactic orientation program now under way — the prevention of states that require a stigmatizing name.

This question of nosology is important because people generally are still not well educated in regard to nervous disorders. They forget the wisdom of the Quaker's statement that "Everybody is queer except thee and me, and sometimes I think thee is a little queer." At best the label of psychoneurosis is dangerous because it tends, in the mind of the person so labeled and in the minds of others, to distinguish and to separate him from the rest of the supposedly normal world.

The psychiatric casualties of this war may be roughly divided into two groups, those suffered by men whose previous integration has been averagely sound and who have broken down due to intolerable circumstances, and by those whose histories reveal evidence of instability before the beginning of their military service. Prognosis is better for the first group, but it is probable that the second group comprises the larger number of the disabled. Rennie and Woodward[9] report that of 380 cases seen at the Rehabilitation Clinic of the New York Hospital, 75 to 80 per cent gave a history of difficulty antedating service.

The work of rehabilitation is not being left entirely to civilian and Veterans Administration resources. Both the Army and the Navy have already instituted treatment in the directions of both reconditioning and rehabilitation. Braceland,[10] in writing of the Navy's project, says:

> It is encouraging to know that in this particular field the Navy has had a rehabilitation plan in operation for well over a year. This program has now expanded to such a degree that the basic idea of treatment and reconditioning is operative from the time the individual becomes a neuropsychiatric casualty on some Pacific atoll or island until the time he is considered recovered or is discharged to the Veterans' Administration facilities for further treatment.

Group therapy, according to the same author, is the method of choice.

That group therapy is effective is the opinion of Dynes, Hamilton and Cohen.[11] They write that, although not all patients are cured, many have left the hospital with an unhostile attitude. They add:

> Many expressed a feeling that they had been treated fairly and had hopes and plans for the future. This contrasts sharply with those patients discharged from the service who return to their homes in an unhappy frame of mind and immediately become candidates for veterans' aid, instead of making an attempt to help themselves.

In the group discussions, as conducted by Dynes and his associates, the members were encouraged to describe their symptoms. The meaning and nature of symptoms were then discussed in relation to personality and its development, anatomy, physiology, emotions and their influence on mind and body. The authors say that the individual patient was not embarrassed, any particularly sensitive points being discussed privately.

In a description of the process of group therapy in an Army hospital, Paster[12] relates that it is usual for the aggressive, extroverted patient to express himself first.

> The timid and the withdrawn then follow with comparative ease. . . . It is remarkable how patients who, when individually interviewed, are reluctant to discuss their terrifying past change their attitude during the group sessions. Surrounded by other patients who manifest symptoms similar to their own, most of them lose their sense of inferiority. They talk much more freely about their painful experiences and reveal the inner turmoil they previously tried to repress.

The value of this therapy is evident in that 85 per cent of the men so treated have been returned to duty, although not as combatants. Part of the value, according to Paster, lies in the patient's finding that he automatically minimizes his personal problems as the latter become a part of the larger group problem. Also the presence of other patients helps to socialize each of them. Paster concludes:

> The favorable response of the patients to the comparatively brief period of treatment [two or three times a week for four to six weeks] corroborates the opinion of many that psychoneurotic reactions arising in combat are not generally deeply rooted. They do not fundamentally represent lifelong problems, but rather symptoms of acute maladjustment to intolerable situations.

Helpful as group or individual therapy may be to a man while he is still in service, partial or apparently complete restoration to mental or emotional health before discharge does not preclude difficulties in making the transition back to civilian life. The success or efficacy with which this adjustment will be made depends on the individual veteran's plasticity and emotional integration and various factors in the society to which he returns. One of the most important elements in this situation is the matter of compensation or pensions for veterans. Unfortunately, many men will accept government aid as long as it may be forthcoming, and thus neurotic reactions will become fixed either for life or for years.

Sinclair,[13] of the Australian Army Medical Corps, who has had comprehensive psychiatric experience in the present war, admonishes:

> The nation is still paying for the neuroses directly or indirectly attributable to the last war. The burden following the present conflict will be far greater. The policy adopted after the last war was to pension the soldier and to treat him at a repatriation centre. It will be a great pity if we repeat that folly. There seems no doubt that to shackle the neurotic to his symptoms and disabilities by a monetary dole is a poor solution to his problem. . . . Society will best support the neurotic repatriated soldier by giving him constructive, creative and sympathetic service, rather than by paying him a fortnightly pension in an endeavor to forget him.

What Terhune[6] has to say on this subject is worth quoting.

> The greatest hazard that exists in treating ex-servicemen who are psychoneurotic is that they are eligible for federal pensions. Once these men have applied for a pension or have secured one, it becomes practically impossible to cure them. Few compensation neuroses recover as long as the compensation continues in effect. It is unfortunate that recent federal legislation makes these patients eligible for pensions, since this very fact will make many confirmed neurotics of individuals who would otherwise recover. Such federal provision was made without consultation with medical authorities familiar with the problem.

The author urges medical societies to fight for new legislation. In dealing with the veterans themselves, he advises the doctor to try to persuade them "not to apply for pensions, pointing out the nature of the risk and showing them that by accepting pensions they are selling their birthright of happiness and usefulness, dooming themselves to lifelong discomfort, all for a mere pittance."

The numerous psychologic hurdles standing in the way of the returned soldier's successful reorientation to civilian life have been well presented at length by Pratt.[2] He discusses the possible obstacles that may be present both in the veteran's attitudes and in those of his family and social milieu. Patience, forbearance and an unremitting attempt to understand are the keynotes for success.

Chisholm,[14] in an excellent paper, outlining the Canadian Army's proposals for preparing its soldiers for demobilization, writes of some of the most important points related to rehabilitation. He says:

> Aggressive urges which have been carefully nurtured and developed over a period of years are supposed to disappear overnight, leaving a peaceful civilian with no such pressures and consequently no need of outlet. The soldier is expected overnight to give up what in very many cases at least is a consuming hatred and in all cases the object of aggressive antagonism. . . . With the memory of . . . his friends or relatives who have been killed or maimed or even tortured by the enemy, fresh in his experience and kept alive as a spur to his aggressions, this change-over in attitude may be very difficult indeed. It may be successful on the surface but at the expense of extensive repressions and conflict within himself.

The well-known tendency of the soldier at war and the wife at home to idealize each other, with perhaps consequent disillusionment; fears of what may or may not have been infidelity; idealization of the father by the mother to the children, at

variance with the real father on his return; the wife's independence, personally and financially, in relation to her husband, while he has been away; the wife's experience in war work, having broadened her horizon beyond the domestic round; the matter of re-employment or employment for the first time in a civilian job for the returned soldier — all or some of these situations may be the source of difficulties. According to Chisholm, the Canadian Army's plan is an attempt to make the soldier's transition to civilian life less uncomfortable and, as so often happens, disillusioning by courses of lectures and discussions in small groups on all conceivably pertinent subjects.

The working and suffering together and the value of their efforts to their countries have given to many soldiers a well deserved self-esteem that may never have been experienced by them before to such degree. The doffing of the uniform and the return to a position of relative unimportance can be a serious threat to healthy adaptation unless families and the community remember that the wisest form of appreciation goes farther than an initial flag-waving reception. In another paper, Chisholm[15] comments on this.

> For some years the soldier will have been accustomed to regarding himself as important, as a great asset to his country and as highly valued by his associates. . . . The most damaging thing that could happen to the returned soldier and to the community to which he returns would be for him to find himself not wanted and not regarded as a valuable asset to the community. To give him money or even to provide him with a stopgap job will fall far short of these requirements. In order for him to become a useful civilian citizen it is very necessary that his own individual value to the community should obviously to him remain high. This will require very careful planning and very generous and serious implementation.

Community responsibility is stressed in the literature on rehabilitation. There is much exhortation about it. Rennie[1] writes, "The whole purpose of psychiatric treatment may even be defeated by the unresponsive or negativistic attitude of the community or industrial employers." Rennie and Woodward[9] are convinced that

> The degree of social adjustment that men returning from the armed forces make and the speed with which they do it depend to a very real degree on the understanding they find among civilians, and on the way the people at home treat them. With understanding, reassurance, and constructive treatment, many of them achieve an acceptable status and carry on quite effectively after an adjustment period of a few weeks or at most a few months.

Farrell[16] also believes that the tasks of rehabilitation are not singly those of the medical profession. He adds:

> Business also has a large measure of responsibility. . . . They must be given every chance and encouraged to make good in industry. It is often remarkable how quickly even some of the most upset individuals return to their former life and efficiency in their productive work once the pressure that broke them can be removed.

The psychiatrist should take the lead, in the opinion of Finesinger and Lindemann,[17] in organizing community resources. They write, "An educational program making available what we have to say to the general medical profession, to community authorities, social agencies, industrial personnel and clergymen should be the concern of our intensive thinking." They state that rehabilitation clinics are rapidly developing in different communities.

As suggested earlier in this review, one of the problems of rehabilitation is the disinclination of men needing help to seek it. Community efforts will have to be enticing to attract the veterans who are not desperate, or not unusually well educated in regard to mental hygiene, or not dependent enough to want and to accept what is offered. Millet[18] is sanguine in this regard. He writes:

> Fortunately, large numbers will have highly constructive or hopeful attitudes toward their disabilities and be eager . . . to take whatever specific retraining is necessary in order to be able to resume a life of self-support and independence. Such men may be counted upon to broaden the understanding of civilians as to the needs of other discharged men, and in some cases will provide excellent material for recruiting as experts in rehabilitation.

In spite of Braceland's[10] charge, "It has been repeatedly stressed by industry as well as by the military services that a man must be fit for all duties or for none at all, and this all or none theory is the psychologic barrier which the returning veteran has to hurdle," it is to the credit of psychiatry and industry that for some years the larger industries, at least, have recognized the value of including psychiatrists or psychiatrically trained personnel directors on their staffs. Employment and employee-employer problems and the personality of the individual worker, as contrasted with the impersonal, exclusively monetary profit motive, had been given consideration and attention from the psychiatric or mental hygiene point of view long before the industrial rehabilitation difficulties of World War II arose.

The principal hazard in the present situation is that industrialists may be influenced by the popular articles of journalism to believe that it is well to be wary of the man who has been discharged for neuropsychiatric disability. How a division of the General Motors Corporation is meeting the issue of rehabilitation in industry is well delineated by Smith.[19] He wrote in April, 1944, that the Delco-Remy Division had been keeping in touch constantly with about 5000 employees in military service. These men were sent letters, and gifts on various occasions, as at Christmas and Easter, and were told that they were wanted back when the war was over. Hundreds of letters had been received each week from the former employees. "Every letter that asks a question or indicates that a reply is desired is answered."

The policy of the Delco–Remy Division is as follows:

> Veterans will be given every possible assistance, sympathy and consideration in helping them to get back into

> the normal swing of civilian life. However, it is not our intention to oversympathize, coddle or lead them by the hand. In our opinion such treatment will simply lead to untold trouble in the future, as it develops in the individual the feeling that he is different from other people, entitled to special considerations, and that the world owes him a living.

This policy includes the decision not to give veterans preferential treatment. Although the plan of setting them apart from the general group of employees was considered, it was decided "that the veteran should, to all outward appearances, be treated as all other incoming employees." Smith states that a great majority of over one hundred veterans questioned on this plan preferred to be considered as no different from their fellows." This is the particular desire of that group of veterans who have been discharged from military service because of some slight mental or physical impairment which made them unfit for life in the service."

At the time Smith's report was written the Delco–Remy Division had employed 475 veterans. It was found that these men fell into two general classes. The first comprised battle-incurred disability discharges and men discharged as unfit for service because of some slight mental or physical disability. The rehabilitation of this class had not proved much of a problem and it was thought it would not in the future. The second class was made up of men who had been discharged because they were temperamentally unsuited for military service. Smith states, "This is the group who are emotionally unstable, and in the vast majority of these cases these characteristics were not acquired in the service but are inherent."

Smith's analysis of this type of veteran and the troubles he initiates is perspicacious. This man was a problem before the war, and now that he is a veteran he is more of a problem than ever, taking advantage of being classified as a veteran. He decidedly wants preferential regard. He can do no heavy lifting because of back injury.

> He has calcified glands in his chest and objects to working in any dusty environment; he has an alleged heart condition and must do extremely light work; or he has defective feet and must sit down. He is the "misfit," and generally you will find that he was a "misfit" in society before he entered the service.

The author sees him as a potential danger to the industrial rehabilitation program. Since the man draws and necessitates attention and supervision, there is the danger that he may become a false symbol of the whole body of veterans. Smith believes that industry does owe these men a fair chance. "We will go even further with them than we would with the ordinary employe." He rightly enough thinks, however, that their rehabilitation is not basically industry's but that of society as a whole. He cautions that it is in relation to this type of veteran that pressure groups may arise. A union may charge that big business is being unfair to an ex-soldier when actually industry is doing all that it can to help an incompetent.

Smith concludes:

> The number of veterans who return with physical or mental impairment will be relatively small in relation to the total in service. . . . This job resolves itself to simply handling each case on an individual basis. . . . taking into consideration capabilities as well as limitations, assisting him to choose the work which he will be able to do best in order that he may be a self-sustaining member of society for the balance of his productive life, . . . doing all this without emotionalism or paternalism — helping him to help himself.

If industry throughout the country could carry out the purported policy of the Delco–Remy Division, it would seem that the veterans' reinstatement would be wisely directed.

To help industry, especially the small and moderate-sized companies, which employ the major portion of American labor, in the work of readjusting service men and women to industrial jobs, the Subcommittee on Psychiatry of the National Association of Manufacturers Medical Advisory Committee has prepared a pamphlet, *Readjustment to Civilian Jobs*. The pamphlet is for distribution to management and contains an explanation of what neuropsychiatric disability means, suggestions for placement interviews and a plan for classification and placement in accordance with the psychiatric and personality impression given by each applicant.

The pamphlet is designed for use not only with the ex-service man but also with the demobilized war worker. It reads in part:

> It is possible that the greater problems will come from the ranks of these war workers. . . . These war industry "employment neurotics" were the product, primarily, of emotional difficulties arising from their failure to adjust to employment requirements and, in many instances, although to a lesser degree, to their failure to adjust to abnormal living conditions in war industrial centers, and to new and unusual social relationships. In attempting to solve their emotional problems, the war-industry neurotics shifted their jobs in large numbers.

The plans for placement consist of estimating the applicant's personality, abilities and disabilities, carried out by a consulting psychiatrist or personnel director, or, if neither of these is available, by the company doctor or the applicant's own doctor, in conjunction with members of the managerial staff; also temporary job placement, providing for "a period of mutual 'on-the-job observation' between the applicant and the employer," when there is doubt about the worker's stability or capabilities.

Comparatively simple as all this may seem, if industry generally could be made aware of the possible value of psychiatric screening and direction, postwar employment difficulties would at least be ameliorated.

There is much literature for public guidance on how the returning service man and woman should be treated. One of the shorter of these, *When He Comes Back and If He Comes Back Nervous*,[20] is suitable for families who may want suggestions or

advice. Besides explaining briefly how and why war experience may change the man who has been in service, it contains a number of sound "do's" and "don't's." Also, Pratt's[2] book, referred to previously, contains a large amount of generally useful information.

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References

1. Rennie, T. A. C. Psychiatric rehabilitation therapy. *Am. J. Psychiat.* **101**:476-485, 1945.
2. Pratt, G. K. *Soldier to Civilian: Problems of readjustment.* 233 pp. London: McGraw-Hill Book Company, Incorporated, 1944.
3. Kubie, L. S. Psychiatric personnel of future. *Digest of Neurol. & Psychiat.* Series XIII, May, 1945. P. 276.
4. Gregg, A. Critique of psychiatry. *Am. J. Psychiat.* **101**:285-291, 1944.
5. Cunningham, J. M. Development of psychiatric service and its relation to returned veteran. *Connecticut State M. J.* **8**:493-498, 1944.
6. Terhune, W. B. Psychiatric problems of returning soldier and their medical management. *Connecticut State M. J.* **9**:29-36, 1945.
7. Burlingame, C. C. Industrial psychiatry — facts — not fancy. *Bull. Massachusetts Soc. Ment. Hyg.* February, 1945.
8. Thomas, J. M. Use of term "Psychoneurosis." *New Eng. J. Med.* **232**:121-124, 1945.
9. Rennie, T. A. C., and Woodward, L. E. Rehabilitation of psychiatric casualty. *Ment. Hyg.* **29**:32-45, 1945.
10. Braceland, F. J. Role of psychiatrist in the general rehabilitation program. *U. S. Nav. M. Bull.* **43**:621-627, 1944.
11. Dynes, J. B., Hamilton, F. J., and Cohen, R. A. Program for rehabilitation of psychiatric war casualties: role of convalescent hospital. *U. S. Nav. M. Bull.* **43**:628-633, 1944.
12. Paster, S. Group psychotherapy in army general hospital. *Ment. Hyg.* **28**:529-536, 1944.
13. Sinclair, A. J. M. Psychiatric aspects of present war. *M. J. Australia* **1**:501-514, 1944.
14. Chisholm, G. B. Emotional problems of demobilization. Read at the annual meeting of the Association for Research in Nervous and Mental Disorders, New York City, Dec. 15-16, 1944.
15. *Idem.* Psychological adjustment of soldiers to army and civilian life. *Am. J. Psychiat.* **101**:300-302, 1944.
16. Farrell, M. J. Developments in military neuropsychiatry. *J. Iowa M. Soc.* **34**:387-391, 1944.
17. Finesinger, J. E., and Lindemann, E. Discussion of psychiatric aspects of rehabilitation. *Dis. of Nerv. System* **6**:149-155, 1945.
18. Millet, J. A. P. Honorable discharge. *Am. Scholar* **13**:429:436, 1944.
19. Smith, W. A. Putting the veteran back to work. *J. Indiana M. A.* **37**:282-289, 1944.
20. Rennie, T. A. C., and Woodward, L. E. *When He Comes Back and If He Comes Back Nervous.* 32 pages. New York; National Committee for Mental Hygiene Incorporated, 1944.

CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor**

BENJAMIN CASTLEMAN, M.D., *Acting Editor*

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CASE 31291

Presentation of Case

A sixty-one-year-old man was admitted to the hospital because of fever, chills, malaise and weight loss.

The patient had been well and active until about four months before admission, at which time he began to feel weak and tired. He had sudden chills and fever and remained in bed for several weeks. He took small doses of quinine without consulting a physician. Three months before admission he developed severe spontaneous nosebleeds, for which he was admitted to a community hospital, where he remained for three months. While at the other hospital he ran a septic course, with a chill and a sharp temperature rise to about 103°F. almost every afternoon. It was necessary to pack the nose because of repeated spontaneous hemorrhage. The red-cell count fell from 3,300,000 on admission to 2,400,000 at the time of discharge. The white-cell count varied from 7000 to 15,000, with as many as 93 per cent neutrophils. A platelet count was 65,000, the bleeding time 2¼ minutes, the clotting time 3¾ minutes, and the prothrombin time 20½ seconds. A tourniquet test was negative. The urine was normal. The serum nonprotein nitrogen was 30 mg. per 100 cc. The Hinton and Wassermann tests were negative. X-ray and physical examinations of the heart and lungs were negative. One blood culture showed diphtheroids. Several blood cultures showed *Staphylococcus albus*, and two cultures yielded colon bacilli. Examinations for malarial parasites were repeatedly negative. Tests for agglutinins against typhoid, paratyphoid and dysentery bacilli were negative. He was given sulfadiazine until it was learned that the *Staph. albus* grown from the blood was resistant to sulfonamides. He was given up to 20,000 units of penicillin every hour for several weeks. During penicillin therapy the blood cultures became negative, but he continued to have chills and a fever of 103°F. The teeth, sinuses, nose and throat and the genitourinary system were thoroughly studied by consultants and were said to be negative. An intravenous pyelogram was normal. X-ray films of the bones were normal. Penicillin was stopped, and the blood culture promptly became positive for *Staph. albus*. Sulfadiazine was given in high dosage, and a blood level of 15.2 mg. per 100 cc. was obtained. After two weeks the sulfadiazine was stopped because of hematuria, crystallinuria and a nonprotein nitrogen of 72 mg. per 100 cc. Fluids were forced and the patient became edematous, whereupon the fluids were limited. The urine soon became negative. Considerable abdominal discomfort, of which he had begun to complain, was relieved by enemas. The blood cultures remained negative after the administration of the second course of sulfadiazine until three days before he was discharged, at which time *Staph. albus* was again obtained. Shortly before discharge the serum albumin was 2.15 gm., and the globulin 3.75 gm. per 100 cc., an albumin-globulin ratio of 0.57. This test was repeated, and the albumin was 1.84 gm., and the globulin 4.16 gm. At the same time the serum nonprotein nitrogen

*On leave of absence.

was normal, and the sedimentation rate 1.4 mm. per minute. X-ray films showed marked gaseous distention of the intestines, with a high diaphragm, especially on the right. The temperature varied from 100 to 106°F. Many moist rales were heard in the chest posteriorly. He was transferred to this hospital in an ambulance.

Physical examination revealed a thin, pale, drowsy man who appeared chronically ill. There was moderate pitting edema over the sacrum and of the lower extremities. Respiratory excursions were shallow. The diaphragm was high on both sides. There was dullness at both bases posteriorly, considerably more marked on the left than on the right. Breath sounds and vocal and tactile fremitus were markedly diminished at the left base. Moist crepitant rales were present at both bases. The heart was slightly enlarged to the left. The rate and rhythm were normal. No murmurs were heard, and the aortic second sound was equal to the pulmonic. The abdomen was markedly distended but not tender; there was shifting dullness, but no fluid wave could be elicited. The liver and spleen could not be felt.

The temperature was 99.0°F., the pulse 90, and the respirations 23. The blood pressure was 165 systolic, 105 diastolic.

Examination of the blood showed a red-cell count of 2,400,000, with 7 gm. of hemoglobin, and a white-cell count of 9800. The differential showed 78 per cent neutrophils, 17 per cent lymphocytes, 3 per cent monocytes and 2 per cent eosinophils. The stool was brown, formed and guaiac negative. Serum and spinal-fluid Hinton tests were negative. The urine was cloudy, had a specific gravity of 1.014 and gave a + test for albumin; the sediment contained 3 or 4 red cells, 12 to 20 white cells, with occasional clumps, a rare granular cast and many bacteria per high-power field. An abdominal paracentesis yielded 2800 cc. of light-yellow, slightly hazy fluid. The specific gravity was 1.008, and the sediment contained 115 white cells (mononuclears) and 45 red cells per cubic millimeter. A culture showed no growth. The serum nonprotein nitrogen, chloride and carbon dioxide levels were normal. The protein was 5.13 gm. per 100 cc., with an albumin-globulin ratio of 0.9. The cephalin flocculation test was ++++ in twenty-four hours. The prothrombin time was 24 seconds (normal, 18 to 20 seconds). A bromsulfalein test showed 60 per cent retention forty-five minutes after 5 mg. of dye per kilogram of body weight had been injected. A blood culture yielded no growth. The urine grew abundant colonies of colon bacilli. An x-ray film of the chest showed the right half of the diaphragm to be high in position, but both sides moved well. The liver was thought to be considerably enlarged. There were areas of increased density in the right middle and lower lobes. The heart was prominent in the region of the left ventricle. A gastrointestinal series was negative.

The patient felt weak and frequently became flushed. The paracentesis relieved him completely of a moderate amount of dyspnea. He ate poorly, frequently refusing a meal. He was given four transfusions and frequent intravenous injections (dextrose, Amigen and physiologic saline solution). During the first week he showed a low-grade fever, the temperature rising to 101°F. every evening. During the second and third weeks the fever was more erratic, with daily spikes sometimes reaching above 103°F. The pulse and respirations spiked with the temperature.

On the third day the liver was palpable two finger-breadths below the costal margin. On the fourth day the patient complained of a stiff neck. A lumbar puncture revealed normal spinal fluid, except for a gold-sol curve of 5554333100. Peritoneoscopy showed a normal-appearing liver that did not seem to be enlarged; the peritoneum was smooth. A liver biopsy showed no abnormality.

On the tenth day he again became markedly dyspneic. On the following morning he complained of sharp pain in the right chest anteriorly. The right dome of the diaphragm was found high and considerably more elevated than the left. Breath sounds in the right lung field were markedly diminished, and a moderate number of fine moist rales were heard. Examination of the legs was negative except for edema. An abdominal paracentesis yielded only 100 cc. of fluid. An x-ray examination of the chest showed considerable change since the observations made shortly after admission. The right lower lung field was diffusely hazy, and there was evidence of fluid within the pleural cavity. It was impossible to determine the position of the right leaf of the diaphragm. At the same time the urine contained innumerable white cells, many in clumps, and bacteria. The white-cell count was 36,500, with 9 gm. of hemoglobin. The stool was for the first time guaiac positive. There was no pain or tenderness in the abdomen or back.

On the sixteenth day the patient became incontinent and spoke in a disoriented fashion. Weakness and weight loss progressed. After several transfusions the serum protein was 6.1 gm. per 100 cc. The nonprotein nitrogen, chloride and van den Bergh remained normal. The white-cell count on the twentieth day was 21,000, with 94 per cent neutrophils. He became severely dyspneic again and slightly cyanotic and was relieved somewhat by an abdominal tap, which yielded 1800 cc. of thin yellow fluid. No fluid was obtained by thoracentesis.

On the twenty-second day the chest began to fill with fine rales and wheezes. Severe dyspnea returned. The pulse was 120. He was digitalized rapidly with Cedilanid. When pulmonary edema became alarming, he was given oxygen and tourniquets were applied to the extremities. The following morning he went into peripheral collapse and expired.

Differential Diagnosis

Dr. Wyman Richardson: As usual I have two possibilities in mind. Was this primarily infection or primarily tumor, possibly with secondary infection? This time I am going to rule out tumor as a primary cause of the disease because the only one I can think of as a possibility is lymphoma, and the whole course of the disease seems to be more that of infection. The thing that bothers me a little is the rapidly increasing anemia in the beginning, which is perhaps more than one would expect with ordinary infection, although it is possible.

This case brings up the question of how much to believe the evidence from a hospital with which we are not familiar. I do not wish to be "stuffy" about that, but when one is around a hospital, one realizes the difficulties of the laboratory and has opinions about the methods employed and whether or not the laboratory procedures can be considered important or reliable. There is some discrepancy between the laboratory findings at the other hospital, and one finding in particular, the positive blood culture for *Staph. albus*, deserves attention. *Staph. albus* showed up with great regularity when the patient was in that hospital. In this hospital, apparently the physicians in charge were not too interested in the blood cultures because only one is noted, at least in this protocol, and that was negative. So I am left a little in doubt whether to take the finding of *Staph. albus* seriously. It is a frequent contaminant. On the other hand if it appears in two flasks regularly, following a rigid technic, one has to believe it. The question is, When does one begin to believe it?

The other thing that I want to comment on in regard to the original laboratory work is the platelet count of 65,000, with a normal bleeding time and tourniquet test. I teach the students in the course in laboratory diagnosis that the platelet count is not worth doing. I believe that is true. The reports of technicians who have spent a lifetime doing these counts are of some value, but as they are usually done they cannot be depended on. One can look at blood smears; if the platelets are diminished, allowance being made for the number of red cells, one can arrive at some definite conclusion. When the platelets are normal in number they clump and cannot be counted. I do not believe that the platelet count of 65,000 is important.

This whole story sounds primarily like infection to me. We might try to tackle this problem from the organs chiefly involved, that is, the kidneys, liver and lungs. The x-ray studies of the lungs at the first hospital were negative, but later there was something that suggested difficulty involving the chest. Involvement of the kidneys appeared right after the patient had been on sulfadiazine for a considerable period of time, and involvement of the liver came on after that period, so that one begins to think of the possibility of some sort of infection, perhaps complicated by the use of large amounts of sulfonamides. That is about as far as I can go with the case. I have come to a conclusion in regard to what this infection might have been, but I think that I should like to look at the chest plate now. I might say that what I am thinking of is whether this man had thrombophlebitis with septic infarcts, whether he had phlebothrombosis with noninfected infarcts, whether he had multiple abscesses in the lungs, whether he had pulmonary tuberculosis or some such process or whether he had atelectasis from a high diaphragm.

Dr. George W. Holmes: I think that we can rule out a few of the possibilities. I do not believe there is any evidence of miliary tuberculosis or anything resembling it. I do not believe that he had miliary abscesses in the lungs, or abscess of any kind. There is a high diaphragm on the right side; if one can believe the report that it moved freely, it was probably due either to a large liver or to some degree of atelectasis. There is a line running out just above the diaphragm that could be the end result of localized atelectasis, but it is not definite. The heart, I think, is perhaps within normal limits. Because of the high diaphragm on both sides the heart lies horizontal in the chest and therefore seems larger than it is. The curve of the left ventricle is a little prominent, and he may have had some enlargement of the left side of the heart. The aorta shows tortuosity, but no more than what a man of his age should have. There is no calcification in the walls, and no evidence of mediastinal tumor.

The films taken about a week later show increased density on the right side of the chest and what looks like fluid in the pleural space, perhaps with consolidation in the lung fields. One wonders if this could have been a terminal affair. The left lung still shows no essential change. The heart has rotated a little so that it may be slightly displaced, but I doubt it. Evidently this film is an attempt to see whether or not he had esophageal varices. There is no evidence that he had them. There is nothing in the examination of the stomach; it was said to be negative, and what films we have confirm that.

Dr. Richardson: I am still in a quandary. Incidentally, we have no history of injury to account for a portal of entry for this organism, which is important. Dr. Castleman tells me that the patient was a Greek, born in Greece. What was his occupation?

Dr. Benjamin Castleman: He was in the tonic business.

Dr. Richardson: Perhaps he took too much of his own tonic. Some Mediterranean people have a tendency to liver disease. I do not believe that we have to consider echinococcal disease in this case.

So it comes down, as far as I am concerned, to a blood-stream infection without any obvious portal of entry to account for the illness before he arrived in this hospital, and I am inclined to take the blood culture of *Staph. albus* seriously, in that it appeared

to be somewhat affected by therapy. I think that the history suggests that he had pulmonary infarcts. We know that a partial collapse of the right lung base, with fluid, is not an infrequent finding in the presence of abdominal fluid and liver disease, and that may be the whole explanation. We know that he had a urinary-tract infection and have to say that he had a pyelonephritis. The question is whether that is the only lesion or whether there are others.

I am still trying to decide whether he had thrombophlebitis from the onset. I think that I shall accept *Staph. albus* septicemia as the diagnosis in the first hospital; as a result of the septicemia, he may have had abscesses elsewhere, including renal abscesses. I believe that he was given sulfonamides in proper doses, but he had had them for such a length of time that toxic effects may have occurred; therefore I shall have to bring up the question of a toxic effect on the kidneys.

Finally, one has to explain the liver. There is no evidence of liver infection that I can see. There seems to be evidence of diffuse involvement of the liver. I might parenthetically state the evidence for that: a 60 per cent retention with a large dose of bromsulfalein, a ++++ cephalin flocculation test, a reversal of the albumin-globulin ratio, with a quite marked increase in the globulin at the other hospital (the total protein had gone down when he reached this hospital, but he still had increased globulin here), slight increase in the prothrombin time (probably of no significance), and ascitic fluid that was a transudate rather than an exudate. It is possible to suggest that this man had a toxic involvement of liver as a result of the sulfonamides. It is, however, a rather rare condition, and I assume that this man had some underlying liver disease to start with.

I shall say specifically that this man had a bloodstream infection, possibly due to *Staph. albus*, pyelonephritis, possibly multiple abscesses, pulmonary infarction and toxic hepatitis superimposed on cirrhosis.

Dr. J. H. Means: We struggled with this diagnosis in much the same way that Dr. Richardson has. The patient was desperately ill when he entered, although he was not running a fever. Later he ran a septic fever. In my first note, I said: "I cannot make a diagnosis. He has, I believe, some undrained pus somewhere. At least it must be searched for. There is considerable evidence of liver involvement. He could have a liver abscess." Then we thought of lymphoma, and I stated farther along that the studies were indicated, especially of the liver. Just as Dr. Richardson thought, because of the 60 per cent dye retention, the ++++ cephalin flocculation test, the low albumin-globulin ratio and so forth, I made this note, "If it is cirrhosis, the hair-on-the-chest rule will have been broken because he has plenty of it." A liver biopsy was said to be negative. Still later I wrote that the patient had been running a fever since the punch biopsy, had a leukocytosis and had developed right pleural effusion, and I wondered if there was any relation between the procedure and the subsequent events. We never established that there was. I begged the surgeons to search for pus somewhere, but I could not sell the idea to them. That is as far as we got.

The final diagnoses were liver disease and urinary-tract infection; we thought that the signs in the lungs were due to pulmonary edema. We investigated the urinary tract, colon and gall bladder in the hope of making a diagnosis, but that is as far as we got. We thought that he had liver abscess in all probability. He did not have meningeal signs, and a lumbar puncture was negative. Dr. Benedict saw no peritoneal lesions when he did the peritoneoscopy, and he could not establish anything in the lymphoma category.

This will turn out to be an interesting case. I know that it brings up the point that one will not make the correct diagnosis unless one thinks of all the possibilities. The past history was talked about a little, but insufficiently. We obtained no history of what would have given the clue to what the pathologist found. If we had gone at it harder and perhaps more expertly, we might have got it, but the patient was said to have been well until the sequence of events that led to his death began.

Dr. Francis D. Moore: At the time that I saw this patient the problem was whether he had right subdiaphragmatic abscess, either secondary to some focus that was back of the whole disease picture or secondary to peritoneoscopy, following which he developed more fever. It was difficult to settle the matter one way or the other. He did not have much tenderness in a region of the right eleventh and twelfth ribs and there was none in the upper quadrant. As a matter of fact, in relation to the final proved diagnosis, the absence of abdominal signs in either hospital, other than the signs of fluid, was interesting. At the time that I saw him I was not sure that he did not have subdiaphragmatic abscess. He was much too sick to explore.

Dr. Means: I was not being critical. We thought it was good judgment on your part. I am trying to throw out the thought that we did bring up the possibility that he had pus that could have been drained and asked the surgeons about it. We could have been criticized had we not done so. At entry he had some suggestion of ileus, but it did not amount to much.

Dr. Richard H. Sweet: Was there any history suggesting antecedent appendicitis?

Dr. Means: None that we could obtain.

Clinical Diagnoses

Pyelonephritis.
Liver disease (? abscess).
Pulmonary edema.

Dr. Richardson's Diagnoses

Septicemia (? *Staph. albus*).
Pyelonephritis.
Multiple abscesses?
Pulmonary infarction?
Toxic hepatitis, with underlying cirrhosis?

Anatomical Diagnoses

Periappendiceal abscess, chronic.
Peritonitis, acute fibrinous, pelvic.
Thrombophlebitis of superior mesenteric, splenic and portal veins (pylephlebitis).
Liver abscesses, multiple.
Pancreatic abscesses, multiple.
Abscess, lesser omental sac.
Ascites.
Bronchopneumonia.

Pathological Discussion

Dr. Castleman: The autopsy on this man showed a lot of fibrin and pus in the pelvis that was well on its way to organization. The upper abdominal cavity contained about a liter of clear fluid. The liver was slightly enlarged, and between the head of the pancreas and the right lobe of the liver was a large abscess that extended into the pancreas. Smaller abscesses were scattered throughout the entire pancreas. When the liver was sectioned we found two or three large abscesses, but the most striking finding was in the venous system. The main portal vein and all its radicles were filled with pus and purulent thrombi. These thrombi had extended into the splenic and superior mesenteric veins. We looked then, of course, for the appendix, since it is well known that pylephlebitis is most frequently caused by acute appendicitis. The appendix was extremely small and covered with fibrous tissue and rather porky, fatty tissue. There was no evidence of acute inflammation, but we thought that it might well have been the source of the pylephlebitis a month previously. Microscopically the appendix showed a chronic process. It is conceivable that the abscesses in the pancreas might have had something to do with the production of the pylephlebitis, but I rather think they were secondary to the abscesses in the liver. There was a pyelitis and a mild pyelonephritis. The lesions in the lungs proved to be bronchopneumonia.

Dr. Richardson: What was the organism?

Dr. Castleman: We cultured the abscesses of the liver and found nonhemolytic streptococci and *Staph. albus*, and from the blood we obtained nonhemolytic streptococci and colon bacilli. I think that perhaps the staphylococcus was not a red herring.

Dr. Moore: This boils down to the question whether acute appendicitis can give pylephlebitis without rupture or without being gangrenous.

Dr. Castleman: The appendix might have ruptured. It was extremely small, and we could not find a definite tip. It is possible that the tip had completely organized over a period of several months. The fact that the infection that we did find in the abdominal cavity was located in the pelvis points more to the appendix than to any other organ. There were several loops of small bowel adherent to the exudate in the pelvis, but there was no abnormality in the intestinal tract.

Dr. Means: I should like to ask the surgeons whether anything could have been done if the diagnosis of suppurative pylephlebitis had been made when he first came in.

Dr. Sweet: Nothing, unless one is dealing with a large single abscess, which is not the case in pylephlebitis.

CASE 31292

Presentation of Case

A twenty-day-old male infant was admitted to the hospital because of vomiting and diarrhea.

The infant was born at term, weighing 7 pounds, 2 ounces. The delivery lasted one hour. The mother said that the baby had vomited before it was discharged from the maternity hospital but there were no other feeding difficulties. At home the formula consisted of 12 ounces of whole milk, 10 ounces of water and 3 tablespoons of Karo. Vitamins A, C and D were given in adequate amounts. The baby fed well but vomited each feeding a few minutes after it had been taken. The parents were not certain that the vomiting was projectile. Proper belching did not prevent vomiting. The infant had six to seven bowel movements a day, which were green and liquid. The mother stated that the baby had had a rash on the buttocks when he left the hospital and that she thought that he had had diarrhea while in the hospital. Two days after the baby arrived at home, his formula was changed to skimmed milk and water, with no improvement. A few days later Dextri-Maltose was added, to be omitted again after a few days. The baby had lost 1 pound, 2 ounces, before admission.

Physical examination revealed a dehydrated infant who was ashen gray. The anterior fontanelle was sunken. The child measured 20½ inches and weighed 6 pounds. There was a marked rash on the buttocks. The ears, nose and throat were normal. The lungs were clear to percussion and auscultation. The abdomen was soft, and the umbilicus showed a slight serous discharge. Peristalsis was normal. No masses were felt. The extremities were normal.

The temperature was 99.0°F., the pulse 130 and strong, and the respirations 34.

Examination of the blood showed a red-cell count of 4,500,000 and a white-cell count of 18,700. The stools were liquid and green and contained no blood. The urine was normal. The blood was Type O,

Rh+. The serum nonprotein nitrogen was 22 mg. per 100 cc., and the protein 3.4 gm.

The child was given nothing by mouth, being fed parenterally. He was started on sulfadiazine as soon as hydration was established, and from the next day on he was also given penicillin. He continued to have small green stools. A lumbar puncture was negative, and culture of the cerebrospinal fluid showed no growth. After forty-eight hours on parenteral-fluid therapy, he was given skimmed milk and Karo by mouth. Within ten hours the number of stools increased to such an extent that these feedings were promptly discontinued. No pathogenic organisms were grown from the stool. A culture of the discharge from the umbilicus grew colon bacilli. A blood culture on admission was contaminated, and one on the fifth day showed no growth. Cultures from the nose and throat showed chiefly *Staphylococcus aureus*. The sulfadiazine level, based on two determinations, was about 5.0 mg. per 100 cc.

The child seemed greatly improved on the fourth day. Physical examination showed that he was well hydrated. The nose, throat, ears, lungs and urinary tract were negative for signs of infection. The rash on the buttocks had cleared, and there were three small dark green stools that day. The temperature had continued to be normal since admission.

The next morning the child suddenly became cyanotic and went into circulatory collapse. The extremities were cold. The respirations were 22 but were labored, with some sternal retraction. The heart sounds were of poor quality. The abdomen was distended, and the liver was not enlarged. Peristalsis was normal. The stools, which had been guaiac negative, became positive. X-ray examination of the chest and abdomen was negative. The child was given plasma, 10 per cent dextrose in water and physiologic saline solution intravenously and was placed in an oxygen tent. The white-cell count on the fifth day was 3250, with 75 per cent neutrophils; the hemoglobin was normal. Three hours before death, bilateral swelling was noted over the mastoid region. The eardrums appeared normal. The temperature, pulse and respirations continued to be normal. The child expired quietly on the evening of the fifth day.

Differential Diagnosis

Dr. Dario Morelli: Before we attempt to arrive at the cause of vomiting and diarrhea in this infant, I should like to comment on one point which to me is exceedingly important and which has been omitted, that is, the details of the birth. A great deal of information can be derived from points concerning the type of birth, the condition of the baby at birth and the immediate postnatal as well as the neonatal period. We are told that the infant was born at term and weighed 7 pounds, 2 ounces, and that the delivery lasted one hour. This is quite a long time for delivery, unless it is meant to indicate the whole period of labor. Obviously they must have had some difficulty in the delivery of this child, if delivery is interpreted as the second stage. It was probably a dystocic one, and the possibility of some injury in the process of being delivered has to be kept in mind. We do not know, however, what the condition of the baby was immediately following birth, and so far as the neonatal period is concerned, we have only some vague statements from his mother. She thought that the child might have vomited and that he might have had diarrhea while in the hospital.

At home the vomiting increased to such an extent that he was vomiting after each feeding and the diarrhea was rather marked. The various causes of vomiting in an infant vary from trivial conditions to some which represent serious disease. I am sure that we can rule out most of them very easily.

Air swallowing is one of the very frequent causes of vomiting and that mechanism is quite clear. If the baby swallows air during the taking of food, the air bubble is quite readily expelled and may bring with it food previously ingested. Also, too frequent feedings or too large a volume of food given at one time may cause vomiting. Undue manipulation, improper handling of the baby and unsuitable composition of food have been mentioned as causes of vomiting. Then we have vomiting due to obstruction, such as pyloric stenosis, or obstruction in the intestine, such as intussusception or atresias in the duodenum or in other portions of the intestine. Allergy, pyloric spasm and intracranial lesions are also responsible for vomiting in children. In evaluating the causes of vomiting in this child, his feeding seems to have been adequate and the formula well constituted. We do not know the interval between feedings. but we assume that they were offered every three or four hours. The child was apparently "bubbled up" carefully. We can rule out air swallowing: even if he did swallow air, the mother took care in getting it out of the stomach. We can rule out pyloric stenosis: there was no visible gastric peristalsis, the vomiting was not known to be projectile, and there was no constipation. Intestinal obstruction seems unlikely in that he was having a great number of stools; furthermore, the course of the child's illness certainly does not suggest it.

So we are left with two possibilities, an intracranial condition and a parenteral infection. Parenteral infections are often the cause of vomiting in childhood, especially at the onset of the condition. Before we go any farther with the vomiting let us consider the causes of one of the other symptoms that this child presented, that is, the diarrhea. Unsuitable composition of the food is one. There are a great variety of specific enteric infections, such as bacillary dysentery, typhoid fever and paratyphoid fever, and there is also the extremely im-

portant group of parenteral infections that cause diarrhea in the newborn or in the small child. It immediately emerges from these few considerations of the possible cause of vomiting and diarrhea that we have one condition common to both — parenteral infection. As a matter of fact he was so treated after he first came to the hospital. Very wisely they hydrated him before starting sulfadiazine. The sulfadiazine was followed by penicillin. There is no question that the attending physicians were thinking in terms of infection, and they instituted a careful search for the location of the infection. Apparently the upper respiratory tract was normal. The urine was negative. The ears, throat and nose were said to be normal, although some reservation can be made at this point. I do not doubt the sincerity of the observation but it is known that examination of the throat and ears in a dehydrated infant is certainly a difficult task, not so far as accessibility is concerned but because the appearance of these structures may be quite changed by the dehydration and the throat may not appear infected when it is. We know that often even the most experienced observers have difficulty in deciding whether or not the throat is inflamed in any given case. The same can be said in reference to the ear. Apparently this baby was treated for infection, and the likeliest one was parenteral. The stools did not grow any pathogenic organisms.

Another interesting point is that he had a discharge from the umbilicus. A moderate discharge from the umbilicus is often seen and may be totally insignificant. Certainly a minimal amount of infection is present in a great number of infants and does not constitute any threat to the child's health. It is only when there is infection that spreads to the neighboring tissues causing cellulitis; when this has happened, if the umbilical veins are not fully thrombosed, as in the first two or three days of life, infection may spread through them and cause a general sepsis and involvement of the peritoneum. However, the growth of colon bacilli in a culture from that discharge is probably not significant, but it may indicate something more important than what we are willing to ascribe to it. It is unfortunate that the blood culture on admission was contaminated. It would have been of tremendous importance in deciding whether or not he had sepsis. It was repeated on the fifth day, but by that time the child had received quite a bit of penicillin and one wonders if a positive culture had been affected by the treatment.

The rash on the buttocks is to my mind not specific. It is not described and is only classified as marked. It may have been due to the enormous number of stools that the child was having. It may have been the expression of a simple "diaper dermatitis." The rest of the skin was apparently normal. The rash, however, cleared up after the baby had been in the hospital for four days. One wonders if better care had contributed to that improvement. I think the crux of the whole case is deciding whether this baby had an infection and, if he had, whether it was a parenteral infection or an infection somewhere else; also, whether he had a birth injury, and finally, what caused the baby's death.

I have little doubt that this baby had infection, with vomiting and diarrhea, and it gives me courage to note that in the hospital they apparently thought the same way and treated him for infection. The possibility of birth injury is suggested to me by the fact that delivery lasted one hour. If it was a breech delivery one could speculate on the possibility of intracranial injury, as well as injury to the adrenal glands. At least it is an interesting point to consider. We finally come to the fact that the child had apparently been almost cured. On the fourth day the baby was greatly improved: he was well hydrated, and he did not show anything wrong on physical examination. The stools were few, although the abstract does not say whether they were loose or were formed; possibly they were formed. The next morning he suddenly had a dramatic episode of cyanosis and respiratory collapse. I have been thinking strongly in reading this history of the possibility that I just mentioned — injury to the adrenal glands. We know that the adrenal glands at birth are extremely vascular and highly friable. They are easily damaged and respond to infection in a dramatic way. They may become the site of massive hemorrhages, which manifest themselves with a picture of circulatory collapse, cyanosis, difficult breathing and distention of the abdomen. Hyperthermia and cutaneous hemorrhages may or may not be present. Certainly one should entertain that possibility, and I cannot erase it from my mind, even though I may be wrong in the last analysis.

There is another point of interest in that three hours before death bilateral swelling was noted in the mastoid region. At birth, pneumatization of the temporal bone has barely begun; there exists only one cell, — the mastoid antrum, — and the mastoid process is undeveloped. Development takes place some time later. The antrum is frequently the site of infection, especially following middle-ear infection, which in turn we can say is one of the most frequent findings in infants with acute nutritional disturbances. It sounds to me that this bilateral swelling might well have indicated subperiosteal abscesses in the regions of the antrums. That possibly ties up with the fact that we believe that the child had infection, which caused the vomiting and diarrhea, and that he possibly had a birth injury, and I daresay that possibly his death was due to massive adrenal hemorrhage.

DR. ALLAN M. BUTLER: I certainly agree with Dr. Morelli regarding parenteral infection in a youngster like this. We have a clue to infection in the um-

bilicus, namely, the culturing of colon bacilli at three weeks of age. There are two questions concerning specific bits of information that I should like to ask: What did the urine show in terms of white cells and culture? What was the contaminant in the blood culture?

DR. BENJAMIN CASTLEMAN: The urine was not cultured. It was clear on admission, and the sediment contained 2 or 3 white cells and 2 or 3 epithelial cells per high-power field. The second specimen contained no cells. The blood culture contaminant was *Staph. albus*, in one flask only.

DR. BUTLER: I was wondering if it was a colon bacillus, thinking of colon-bacillus septicemia, where so frequently there are hepatitis, pyelonephritis or infection elsewhere in youngsters of this age.

One might add that the bulging over the mastoid antrums previous to death brings up the whole question of the significance of such infections in many patients of this age group with nutritional disturbances. Way back in 1684 and again in 1920 a great deal of significance was attached to the organisms found at autopsy in such patients. This case received a lot of chemotherapy. It would, therefore, be interesting to know what the cultures from the middle ear and mastoid antrums showed. Such pus has been found to contain almost every variety of organism.

In obtaining the history it would have been important to check with the nursery from which this baby came to see if there was an epidermic diarrhea of the newborn or some such diarrhea as that described by Buddingh and Dodd.[1]

DR. CASTLEMAN: The record states that the mother shared a room with someone else's baby who had the same symptoms.

DR. GERTRUD REYERSBACH: The hospital was called and denied that there had been any diarrhea.

CLINICAL DIAGNOSIS

Diarrhea.
Bronchopneumonia?
Umbilical infection.

DR. MORELLI'S DIAGNOSES

Sepsis.
Suppurative otitis media, involving both mastoid antrums.
Hemorrhage into adrenal glands.
Birth injury?

ANATOMICAL DIAGNOSES

Suppurative otitis media and mastoiditis, bilateral.
Hemorrhage into adrenal glands, bilateral.
Acute enteritis.

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN: At autopsy this baby's middle ears were filled with pus, which had extended into the mastoid antrums on both sides. We cultured the material on one side and recovered colon bacilli. I can find no note about what was recovered from the other side. We cultured colon bacilli from the pleural cavity. In the small and large intestines there were numerous ulcers, those in the large bowel being as large as 6 mm. in length. They were fairly superficial, however, not extending deep into the mucosal layers. Cultures from these ulcers showed only colon bacilli. I do not believe that there is any question that the baby died of sepsis.

As Dr. Morelli suggested, the adrenal glands were involved. The entire medulla of one was filled with blood. It had not enlarged the gland particularly, and was not a really big hematoma, but it probably was sufficient to account for the attack of collapse. The other adrenal gland had merely a few small hemorrhages; this was undoubtedly the same process to a lesser degree. I suppose it fits into the Waterhouse–Friderichsen syndrome, which can occur with any type of infection, not necessarily one caused by the meningococcus. The brain in this case was normal.

DR. BUTLER: Of course this youngster did not respond to intravenous glucose and saline as so many youngsters do who have adrenal difficulty underlying the clinical picture of collapse and dehydration.

As already indicated this case brings up the whole argument of the importance of considering antrotomy in patients with nutritional disturbances and some evidence of middle-ear infection. The argument often given by otolaryngologists is that one does not need to do an antrotomy because the communication between the antrum and middle ear is excellent. On the other hand, Marriott[2] used to say that the communication frequently was not free and that there was an accumulation of pus in the antrum that could not be relieved by opening the middle ear. Did you find as much pus in the middle ear as in the antrum? Was there any evidence of communication between the two?

DR. CASTLEMAN: We found pus in both antrums and middle ears, with good communications between them.

REFERENCES

1. Buddingh, G. J., and Dodd, K. Stomatitis and diarrhea of infants caused by hitherto unrecognized virus. *J. Pediat.* 25:105-113, 1944.
2. Marriott, M. Pediatric aspects of otolaryngology. *Ann. Otol. Rhin. & Laryng.* 37:71-83, 1928.

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CONGRATULATIONS TO THE *HERALD*

In an editorial in the June 24 issue of the *Boston Herald* attention was called to the danger of sensitization to the sulfonamides, even in small doses, when introduced into the body in various ways. It was further emphasized that dressings, ointments, powders and so forth containing such agents can still be bought without a prescription, except in New York City, where the Health Department has banned the indiscriminate sale of these products as well. The *Herald* conservatively states that the free sale of any sulfonamide "complicates practical therapeutics." The promiscuous use of such drugs has certainly created numerous and disabling complications, and the *Herald* is to be congratulated for the emphasis to its readers of the risks of such medication.

This is an excellent example of the way in which the press can disseminate valuable medical information to the public. Possibly this comment was stimulated by a committee of the Massachusetts Medical Society. It is to be hoped so, for to gain the full support of the press in the release of medical facts and figures of value to the citizens of the community is one of the best means of educating the public regarding matters of this sort.

SEVERE PNEUMONITIS CAUSED BY A NEW PSITTACOSIS-LIKE VIRUS

A great deal has been written in recent years about the so-called "virus pneumonias," but little is actually known concerning the etiology of the vast majority of these cases. Few if any of the several viruses that have recently been described have as yet proved to be of etiologic significance in more than an occasional case or a small group of cases. Thus, the virus of ornithosis has been recovered from only a few patients with pneumonia, and the development of antibodies against this agent has been demonstrated in only a few others. In most, if not all, such cases there was a history of reasonably definite exposure to infected birds. The condition is quite analogous in this respect to human infections with the closely related psittacosis virus. The rickettsia of Q fever has rarely been identified as the cause of pneumonia, the notable exception being an outbreak that occurred among the workers at the National Institute of Health.[1] In that outbreak the mode of infection was not definitely established, since those who were afflicted had not been directly exposed to the agent. The rickettsias were being cultured in the laboratory, however, and the pathogenicity of the agent and its mode of spread are such as to make an occurrence of this sort quite possible. None of these agents have proved to be the cause of the large number of cases of primary atypical pneumonias that have been encountered in both the military and civilian populations of this country. Furthermore, the etiologic significance of all the other agents that have been described has not been confirmed.

A recent outbreak of severe pneumonitis in Louisiana[2–5] is of interest because of the finding of a new virus transmissible to animals and apparently spread by contact with infected patients. The epidemic occurred in six isolated communities in the bayou region of Louisiana, the cases being scattered over an area of approximately 20,000 square miles. The disease was recognized as an entity only after an epidemiologic study of 3 cases had been undertaken. It was unusual in that it spread only among nursing contacts and had a high mortality, there being 8 deaths among the 19 recognized cases.

The first case was that of the wife of a trapper, who developed a febrile illness on December 2, 1942; she became progressively worse and was transferred to a sanatorium about 120 miles from her home, where she died on December 18. A nurse who attended this patient and her husband, who likewise helped care for her, both became ill on December 24. The nurse was treated at the sanatorium, where she died on January 6. Before that time, however, she was the source of 6 other cases in nurses and in persons who acted as nurses. The husband became ill after returning home and died on December 26. Of the secondary cases, only the fatal ones spread the disease, and the same was true of subsequent cases. Rigorous control measures were instituted, and after that time, except for an attendant who developed the disease while she was still in quarantine, no further spread occurred. It is of interest that the fatal cases were contagious only during the last forty-eight hours of their disease.

The incubation period was estimated as being between six and nineteen days. Transmission was only through direct contact with cases: no evidence could be found of living or intermediate vector, nor were human carriers or mild cases discovered. There were many possibilities of animal reservoirs, but few of these were adequately explored.

In the course of the epidemiologic studies it was discovered that a similar epidemic had occurred in March, 1936. The clinical picture, as described by the physician who attended the cases, was quite similar. In addition, secondary cases occurred only in the nursing contacts of the fatal cases and there were 5 deaths among the 7 secondary cases that were traced.

The clinical features were characteristic in all cases. The onset was mild, with headache and backache followed by slight chills, sweating and a concurrent abrupt rise in temperature. Pneumonitis was demonstrated early by physical and x-ray examinations. In spite of that fact the patients presented the appearance of well-being throughout the first week and into the second week of their illness and then abruptly went into a state of collapse. This was often accompanied by delirium and cyanosis, and the syndrome sometimes recurred at intervals until recovery or death. The white-cell count was low or normal, only occasionally being slightly elevated. Death usually occurred between the seventh and fifteenth days, and in one case on the thirty-ninth day. The febrile course in those who recovered lasted from two to five weeks. Convalescence in all cases was prolonged, several months usually being required before normal health was restored. Transient alopecia occurred in 3 patients.

Autopsies in 2 fatal cases showed similar changes in each. The lungs revealed sharply defined areas of plum-colored consolidation, an alveolar exudate chiefly composed of large mononuclear cells, hyperplasia of the alveolar lining cells and slight or no involvement of the bronchioles or bronchi. No significant bacteria were found, but a few clusters of minute, basophilic, coccobacillary, cytoplasmic inclusions were seen in the pulmonary alveoli, as well as in the Kupffer cells in one of the cases. The anatomical findings resembled those of psittacosis but showed little in common with those of Q fever.

A virus was obtained from throat washings in 3 of the 4 cases that were tested, and in 2 fatal cases it was also isolated from autopsy material. It was propagated in white mice by either intraperitoneal or intranasal inoculation and in guinea pigs by intraperitoneal inoculation, using either the throat washings or tissue suspensions. The symptoms and gross lesions in animals were similar to those observed with the psittacosis group of viruses, and there were readily demonstrable elementary bodies in stained smears of the spleen, liver and lungs of the infected animals. Guinea pigs respond with a fatal infection, and mice succumb when they are inoculated by any of the usually used routes, that is, intranasally, intraperitoneally, intracerebrally, intramuscularly

or subcutaneously. No other known virus exhibits a similar pathogenicity, and for this reason the virus is probably new.

The possible origin of this new virus in the wild life of the bayou region, its apparent relation to other psittacosis-like viruses, the severity of the disease and the viral spread by contact from fatal cases signify that the virus is an important infective agent. Furthermore, the pathogenicity of the virus for laboratory animals appears to be such as to make it easily recognizable should it be looked for in the future.

References

1. Hornibrook, J. W., and Nelson, K. R. Institutional outbreak of pneumonitis: epidemiological and clinical studies. *Pub. Health Rep.* 55:1936-1944, 1940.
2. Olson, B. J., and Treuting, W. L. Epidemic of severe pneumonitis in bayou region of Louisiana. I. Epidemiological study. *Pub. Health Rep.* 59:1299-1311, 1944.
3. Treuting, W. L., and Olson, B. J. Epidemic of severe pneumonitis in bayou region of Louisiana. II. Clinical features of disease. *Pub. Health Rep.* 59:1331-1350, 1944.
4. Binford, C. H., and Hansen, G. H. Epidemic of severe pneumonitis in bayou region of Louisiana. III. Pathological observations. Report of autopsy on two cases with brief comparative note on psittacosis and Q fever. *Pub. Health Rep.* 59:1363-1373, 1944.
5. Olson, B. J., and Larson, C. L. Epidemic of severe pneumonitis in bayou region of Louisiana. IV. Preliminary note on etiology. *Pub. Health Rep.* 59:1373 1944.

MASSACHUSETTS MEDICAL SOCIETY

POSTWAR PLANNING COMMITTEE

The value of co-operation between physicians, hospital executives and hospital trustees was emphasized at a meeting called by the Postwar Planning Committee on June 20. Representatives of the ninety-eight hospitals in Massachusetts having a capacity of 100 beds or more, including the trustees, the superintendents and the chiefs of the medical and surgical services, met at the invitation of the committee to discuss various aspects of the problems involved in providing adequate opportunities for the postgraduate training of doctors returning from the service at the end of the war, for the extension of postgraduate instruction to all doctors in Massachusetts and for the promotion of health education among the laity. Stimulating suggestions were made by various speakers, one suggesting that a trustee of a large metropolitan hospital, by serving also as a trustee in a hospital at a distance, might bring about an exchange of ideas that would be of benefit to both institutions. It was pointed out that an increase in the number of residencies would also improve the care given to hospital patients.

Among the guests of the committee were nine members of the Massachusetts General Court, who, by their presence, evidenced the increasing interest of legislative representatives in the progressive activities of the Society.

It is to be hoped that this meeting will be followed during the next two or three months by similar meetings in various communities of the Commonwealth.

HOWARD F. ROOT, *Chairman*

DEATH

HAMMOND — William J. Hammond, M.D., of East Walpole, died July 4. He was in his seventy-seventh year.

Dr. Hammond received his degree from Harvard Medical School in 1899. He was a member of the American Psychiatric Association, the New England Society of Psychiatry and the Association for Research in Nervous and Mental Diseases and a fellow of the American Medical Association.

His widow survives.

NEW HAMPSHIRE MEDICAL SOCIETY

DEATH

HILDRETH — Lewis G. Hildreth, M.D., of Marlboro, died June 25. He was in his seventy-eighth year.

Dr. Hildreth received his degree from the Kentucky School of Medicine in 1892.

His widow, a daughter and four sons survive.

MISCELLANY

ALVARENGA PRIZE TO DR. WIENER

In recognition of his important work on the various Rh blood factors and on their genetic transmission, the College of Physicians of Philadelphia, on July 14, awarded the Alvarenga Prize to Alexander S. Wiener. Dr. Wiener will give the Alvarenga Lecture before the College of Physicians of Philadelphia and the Philadelphia County Medical Society on October 3, the title being "Rh Blood Factors in Clinical Medicine."

The Alvarenga Prize was established by the will of Pedro Francisco daCosta Alvarenga, of Lisbon, Portugal, an associate fellow of the College of Physicians, "to be awarded annually by the College of Physicians on each anniversary of the death of the testator, July 14, 1883." The College usually makes this award for outstanding published work, inviting the recipient to deliver the Alvarenga Lecture.

CORRESPONDENCE

MAX MEYERHOF

To the Editor: Word has come from Mizraim. An old doctor died in Cairo, and funeral services were held for him in the Ashkenzai Synagogue on April 23. He was an eye specialist, who also wrote several books on the scientific heritage of the Arabs, according to the obituary column in the *New York Times*. For further identification of the dead, it was mentioned by the newspaper that he was the cousin of a physiologist who had won the Nobel Prize in 1922. Ten short lines, fifty words in all, at the tail end of a narrow column, to summarize the achievements of a long life of scientific research!

Max Meyerhof originated from a family of distinguished scientists and physicians. His maternal uncle was practicing gynecology in Breslau when he was born in Hildesheim on March 21, 1874. Perhaps the memory of his uncle moved him to take up medicine as a profession. He studied at Hannover, Heidelberg, Berlin and Strassburg, where he graduated in 1897. Bacteriology was then a novelty, and young Dr. Meyerhof spent a year (1898) as assistant bacteriologist in the Public Health Institute of Strassburg, studying the biology of the diphtheria bacillus and the mysteries of *Proteus vulgaris*.

This year also brought him closer to his young relative, Wilhelm Spiegelberg, professor of Egyptology at Strassburg University. The lectures of his cousin awoke in him a long-

ing for the land of ancient culture and hieroglyphs. This longing was stimulated further by his postgraduate studies in ophthalmology (1899); at the Berlin and Breslau eye clinics he learned that Egypt is rich not only in hieroglyphs but also in eye diseases. After a preliminary trip to the land of pyramids in 1900, he decided to emigrate from Germany.

In 1903 Meyerhof arrived at Cairo and began his ophthalmologic practice. The next year he was already a member of the Ophthalmological Society of Egypt. Since Cairo is a city of many nations and many languages, where a successful medical practice requires a real linguist, Meyerhof devoted several years to learning Hebrew, Arabic, Persian, Syriac, Turkish and other Oriental languages. These studies brought him closer not only to his patients but also to his colleagues and to the scholars of his adopted land. And the metamorphosis began — Meyerhof, the ophthalmologist, developed into Meyerhof, the medical historian.

During the period of his first stay in Egypt (1903–1914) he was chiefly the eye specialist, the medical practitioner, whose observations and essays filled many pages in the bulletins of his society. He found a veritable museum of eye diseases in his office: purulent conjunctivitis, corneal granulations of all types, eyes affected by leprosy, vernal conjunctivitis, tumors of the eyelids, all types of foreign bodies. He investigated all stages of trachoma, the causes of the disease and its immunological peculiarities, and his interest in this subject remained alive even in his later years.

For his ophthalmologic research he was honored by his Egyptian colleagues, who, in 1909, elected him, the thirty-five-year-old foreigner, to the presidency of the Ophthalmological Society. In this office he showed himself a real benefactor of Egypt by organizing a nation-wide service for the treatment of eye diseases and by establishing an ophthalmologic department at the King's Hospital in 1910.

His frequent visits to the libraries of Cairo, and the stimulating contact with such friends as the scholarly Ahmad Taimur Pasha, led him toward a new field of activity — medical history in general, and the history of ophthalmology in particular. His first medicohistorical study appeared in the 1906–1907 volume of an ophthalmologic journal, and was soon followed by others. He fell in love with Clio, and with the ancient Arabic manuscripts in the Library of the Khedive and in the private collections of Egyptian noblemen. Then, World War I ended his happiness for a period.

His forced volunteering as a physician in the German army resulted in a waste of ten years (1914–1923). After the war, he had to stay in Hannover, where, engaged in medical practice, he waited for a change in the political atmosphere of Europe. In 1923 he was allowed to return to Egypt, only to find part of his library dissipated and some of his notes lost. But he started all over again, this time as Meyerhof, the Arabic scholar and historian. A series of journal articles and books, all of them based on painstaking investigations, is the result of this second period of his productive life.

In 1926 he found the Syriac and Arabic translations of certain treatises of Galen, treatises lost for us, both in the original Greek and in the Latin version. He also showed us the importance of Arab culture in every branch of modern science in the book *Le monde islamique* (Paris, 1926). Two years later, on its centennial celebration, the Egyptian University published his main work, a critical edition of *Ten Treatises on the Eye* (Kitab al-ashr maqalat fi'l-ain), ascribed to Hunain ibn-Ishaq (809–877). By editing the Arabic text with a translation of this rare manuscript, Meyerhof's contribution to science was invaluable, since Hunain's work is not only the earliest existing textbook on the eye and its diseases, but also the starting point of Arabic ophthalmology. For it he justly received an honorary Ph.D. degree from the University of Bonn and an honorary membership in the Royal Society of Medicine in London.

There are many more manuscripts in the old libraries, and from 1928 to 1938 we become acquainted with the work of many other early Arab and Persian physicians, through the researches of Meyerhof: the *Paradise of Wisdom* of Ali at-Tabari (*Isis*, 1921), the ophthalmologic Al-murshid fi'l-kohl of ibn-Aslam al-Gafiqi (Masnou, 1933), the abridged version of the *Book of Simples* of ibn-Muhammad al-Gafiqi (Cairo, 1933–1940) and the pharmacologic work of Beruni (1933). His most widely appreciated finding (1933) is, however, the work of the thirteenth-century ibn-an-Nafis, whom he proved to be the real discoverer of the pulmonary circulation of blood.

The last few years of his life were again disturbed by another world war, and the persecution of his race. His interest turned to Jewish affairs, to the medieval Jewish physicians in the Near East and to that great Jew of the twelfth-century, the second Moses, whose life ended in Cairo, Moses ben Maimun. His Maimonides studies are now left unfinished. Death also spoiled the great ambition of his life — to find the lost manuscript of the admirable work of ibn-al-Haitham on the optics and vision.

In his adopted land he will be remembered as the German doctor who pitied the poor fellahs, with their bloodshot, discharging and blind eyes, as the great humanitarian who organized medical care for a plagued nation's relief. His many friends in the world will soon feel the loss of the foremost historian of medieval Arab medicine, who for many years kept the door of Eastern wisdom open for Western science. With his broad medical background, linguistic knowledge, and love of old moldy manuscripts, he represents to me the ideal medical historian, whose empty home in Cairo now turns into the lost Kaaba of many a planned pilgrimage.

CLAUDIUS F. MAYER, M.D.

Army Medical Library
Washington, D. C.

USE OF THE WORD "ANTIBIOTIC"

To the Editor: It has now been about three years since the terms "antibiotic" and "antibiotic effect" were suggested by Waksman, Horning, and Spencer. The fact that these expressions have gained wide acceptance in a short time shows that they have answered a real need for such terms. There are, however, good reasons for questioning the propriety of limiting the application of so broad and useful a word as "antibiotics" to one particular category of substances that are destructive to life. Certainly many products of the manufacturing chemist, such as the arsenicals and mercurials, and many different types of radiant energy are true antibiotics. The agents that are now being obtained from various forms of bacteria and lower fungi might be referred to simply as bacterial or fungous antibiotics, or from a semantic standpoint the word "mycoantibiotics" has much to commend it. In any event, I venture to suggest that the field of usefulness of the word "antibiotics" should not be circumscribed by conventionally limiting its application to one group of substances alone, especially when from an etymologic viewpoint such restricted use of the term hardly seems justified. Should the word come to be used in a more general sense than being confined to the "mycoantibiotics," then other similar expressions, such as "chemoantibiotics" and "actinoantibiotics," would probably come into use as special group terms.

SPURGEON M. WINGO, M.D.

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BOOK REVIEW

Gynecological and Obstetrical Urology. By Houston S. Everett, M.D. 8°, cloth, 517 pp., with 220 illustrations. Baltimore: Williams and Wilkins Company, 1944. $6.00.

The twenty-three chapters that make up this book offer its readers a review of urology. Anatomy, physiology, diagnosis and treatment are discussed from the experiences of the Gynecological Department of the Johns Hopkins Hospital and University.

It is questionable whether a book of this size can adequately cover the entire field of urology, even when limited to the female patient. Gynecology and urology meet in many conditions, such as urinary fistulas, tumors of the urethra, inflammatory changes and cancer. This common ground is important to both specialists and deserves more consideration than this book provides, since so much space is devoted to urology alone. Much more could have been written on the management of urinary-tract complications that follow operation and on irradiation of the female genital tract.

The author is an enthusiastic follower of the teachings of Hunner, many of whose principles have not been accepted by the average urologist. Those who believe with Hunner, however, will read this book with great satisfaction.

(*Notices on page xvii*)

NOTICES

SOCIETY MEETINGS AND CONFERENCES

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING THURSDAY, JULY 26

FRIDAY, JULY 27

*9:00–10:00 a.m. Medical clinic. Isolation Amphitheater, Children's Hospital.

10:50 a.m. Erythemas. Dr. George Schwartz. (Postgraduate clinic in dermatology and syphilology.) Amphitheater, Mallory Building. Boston City Hospital.

MONDAY, JULY 30

*12:00 m.–1:00 p.m. Clinicopathological conference. Peter Bent Brigham Hospital.

TUESDAY, JULY 31

*9:00–10:00 a.m. Medical clinic. Infants' Hospital.

*12:15–1:15 p.m. Clinicoroentgenological conference. Peter Bent Brigham Hospital.

WEDNESDAY, AUGUST 1

*12:00 m. Clinicopathological conference. Children's Hospital.

*Open to the medical profession.

SEPTEMBER 17. American Public Health Association. Page 752, issue of November 30.

OCTOBER 1–6. Medicolegal Conference and Seminar. Page 776, issue of June 28.

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